A STUDY ON PREDICTION OF PREECLAMPSIA BY MATERNAL SERUM BETA HCG LEVELS IN EARLY SECOND TRIMESTER (13 TO 20 WEEKS) OF PREGNANCY - A COHORT STUDY

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON PREDICTION OF PREECLAMPSIA BY MATERNAL SERUM BETA HCG LEVELS IN EARLY SECOND TRIMESTER (13 TO 20 WEEKS) OF PREGNANCY - A COHORT STUDY "** is the bonafide original work of Dr.S. Vanitha in partial fulfilment of the requirements for MS Obstetrics and Gynaecology branch II examination of the Tamilnadu Dr.MGR Medical university to be held in April 2015 .The period of Postgraduate study and training from June 2012 to April 2015.

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DECLARATION

I solemnly declare that this dissertation **"A STUDY ON PREDICTION OF PREECLAMPSIA BY MATERNAL SERUM BETA HCG LEVELS IN EARLY SECOND TRIMESTER (13 TO 20 WEEKS) OF PREGNANCY - A COHORT STUDY "** was prepared by me at Government Kilpauk Medical College and hospital,Chennai, under the guidance of **Dr. P.S. Jikki Kalaiselvi ,M.D.,D.G.O.,** Professor of the Department of Obstetrics and Gynaecology,Government Kilpauk Medical College and hospital,Chennai. This dissertation is submitted to **The Tamil Nadu Dr.M.G.R. Medical University,Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.S Obstetrics and Gynaecology.**

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CONTENTS

ABBREVIATIONS

ANC	-	Antenatal clinic
AST	-	Aspartate aminotransferase
ALT	-	Alanine aminotransferase
AUC	-	Area under the curve
BMI	-	Body mass index
BP	-	Blood pressure
ELISA	-	Enzyme linked immunosorbent assay
HCG	-	Human chorionic gonadotropin
HRP	-	Horse radish peroxide enzyme
IUGR	-	Intrauterine growth restriction
LMP	-	Last menstrual period
WHO	-	World health organisation

INTRODUCTION

Pre-eclampsia is a multi-system disorder of unknown etiology unique to pregnancy with onset after 20 weeks gestation occurring in 3-8% of pregnancy.[1] Pre eclampsia predisposes to many lethal complications like HELLP syndrome, abruptio placentae, disseminated coagulopathy, eclampsia, acute renal failure and of preterm birth, IUGR, and perinatal mortality.

Therefore it is utmost necessary to diagnose it early. Intensive management of pre eclampsia can prevent many maternal and fetal complications. Intensive obstetric care can be utilized effectively in patient those who are at higher risk of developing pre eclampsia and it will improve the maternal and fetal outcome.

The initiating event in the process of developing pre eclampsia was considered to be the abnormal placentation[38]. Immunological changes occurring in the trophoblasts during mid trimester results in secretary response and it is seen as rise in serum beta hCG levels.

Berg and colleagues(2003) reported that pre eclampsia complications accounts for about 16% of maternal deaths and more than half of it are preventable.

Therefore prediction of preeclampsia in early gestation is of utmost importance to detect and to intervene in the management of high risk pregnancies much earlier to reduce the maternal death and fetal mortality and neonatal morbidity.

AIMS

To study the role of maternal serum beta hCG for the prediction of pre-eclampsia by measuring at 13 - 20 weeks of gestation .

Primary objective:

1. To determine whether maternal serum beta hCG levels at 13-20 weeks gestation can predict pre eclampsia and does it correlates with severity of pre eclampsia.

Secondary objective:

1. To find the associated risk factors in patients who developed pre eclampsia.

STUDY POPULATION

This is a population based cohort study. My study population included total number of 200 antenatal women attending ANC clinic , department of obstetrics and gynecology, Kilpauk medical college hospital, chennai .They were selected according to the inclusion and exclusion criteria's. This study was conducted from March 2013 to December 2013.

Inclusive criteria :

Pregnant normotensive, nonproteinuric women was randomly selected from the gestational age of 13 to 20 weeks of pregnancy irrespective of parity.

Exclusion criteria

1. Multiple pregnancy
2. Congenital fetal malformations
3. Chromosomal disorders in fetus
4. Women with chronic hypertension

5. Diabetes mellitus complicating pregnanc

6. Heart disease complicating pregnancy

7. Women with renal disease.

8. Molar pregnancy

9. Gestational age < 13 and > 20 weeks

- A detailed history was taken about her name, age, address, height, pre pregnancy weight, socioeconomic class ,obstetric score, stress score, past history of preeclampsia and family history of preeclampsia.

- Thorough clinical examination was done .

- Laboratory investigation was done , includes basic hematological investigations, urine albumin and maternal serum beta hCG was estimated by ELISA technique.

- Informed consent was obtained from all subjects.

- Early ultrasound measurement of crown-rump length of the fetus and reliable menstrual history dates were used in gestational age calculation.

- The study subjects were followed once a month till 28 weeks of gestation , once a fortnight till 36 weeks , and once a week till delivery and observed for development of pre eclampsia.

- During each visit she was examined thoroughly including blood pressure , urine albumin , pedal edema and fetal well being is assured.

Pre eclampsia is defined as hypertension more than >140 / 90 mmhg after 20 weeks of gestational age [2] with proteinuria in a previously normotensive and non proteinuric woman on two occasions at least 6 hrs apart.

Proteinuria is defined as $\geq$ 300mg/24 hrs ,a urine protein: creatinine ratio of > 0.3 or persistent 30 mg/ dl (1+ dipstick) protein in random urine samples[3].

SAMPLE SIZE

Sample Size for Frequency in a Population

Population size(for finite population correction factor or fpc)(*N*):	1200
Hypothesized % frequency of outcome factor in the population (*p*):	15%+/-5
Confidence limits as % of 100(absolute +/- %)(*d*):	5%
Design effect (for cluster surveys-*DEFF*):	1

Sample Size(*n*) for Various Confidence Levels

Confidence Level(%)	Sample Size
95%	169
80%	79
90%	124
97%	201
99%	265
99.9%	379
99.99%	471

Equation

Sample size n = **[DEFF*Np(1-p)]/ [($d^2/Z^2_{1-\alpha/2}$*(N-1)+p*(1-p)]**

So, My sample size is 200 (adding 30 more for lost to follow up and other causes).

BLOOD PRESSURE MEASUREMENT[14]

Once the patient was selected by the above criteria the BP has been recorded in the following manner.

1. Having the women rest silently and comfortably for 10 minutes or longer rest period.

2. Blood pressure can be taken whether the patient is sitting or in left lateral position with the arm resting at the level of the heart.

3. Measured with appropriate size cuff , the bladder of cuff should be centered over the brachial artery and its lower edge should be within 2.5 cm of the antecubital fossa.

4. The cuff should be inflated 20 mm hg higher than the pressure at which the radial artery pulse disappears.

5. Blood pressure is measured by listening over the brachial artery using bell of the stethoscope exerting minimal pressure over the skin.

6. Diastolic blood pressure is determined as the disappearance of the sound (korotkoff V). If the sound persists when the cuff deflated then use muffling of the sound (korotkoff IV).

7. Women diagnosed as hypertensive when the BP is ≥ 140/90 mmhg on atleast two occasions atleast 6 hrs apart.

ANTHROPOMETRIC METHADOLOGY

Patients Body mass index was calculated with pre pregnancy weight and height - the Quetelet index.

Body mass index = weight in kg /(height in meters)^2

WHO classification of obesity [15]

CATEGORY	BMI
UNDER WEIGHT	**< 18.5**
HEALTHY WEIGHT	**18.5 - 24.9**
OVER WEIGHT	**25 - 29.9**
MODERATE OBESITY	**30 - 34.9**
SEVERE OBESITY	**35 - 39.9**
MORBID OBESITY	**> 40**

STRESS SCORE[16,17]

COHEN PERCEIVED STRESS

The questions in this scale asks about the feelings and thoughts during the last month. It is indicated by circling *how often* felt or thought a certain way.

How often you have felt or thought the following ways during the last month duration?	**Never**	**Almost Never**	**Some times**	**Fairly Often**	**Very Often**
1.Have ever been upset because of something that happened unexpectedly?	**0**	**1**	**2**	**3**	**4**
2. Felt that you were not able to control the important things in your life?	**0**	**1**	**2**	**3**	**4**
3.Have u felt nervous and "stressed"?	**0**	**1**	**2**	**3**	**4**
4. Felt confident about your capability to handle your personal problems?	**0**	**1**	**2**	**3**	**4**
5. Felt that things were going your way?	**0**	**1**	**2**	**3**	**4**

How often you have felt or thought the following ways during the last month duration?	**Never**	**Almost Never**	**Some times**	**Fairly Often**	**Very Often**
6. Found that you were not able to cope with all the things that you had to do?	**0**	**1**	**2**	**3**	**4**
7. Been able to control irritation in your life?	**0**	**1**	**2**	**3**	**4**
8. Felt that you were on top of things?	**0**	**1**	**2**	**3**	**4**
9. Been angered because of things that were out of your control?	**0**	**1**	**2**	**3**	**4**
10. Felt difficulties were piling up so high that you were not able to overcome them?	**0**	**1**	**2**	**3**	**4**

Total scores may ranges from 0-40. The higher scores indicates greater perceived stress.

0-10: Relatively Stress Free

11-20: Low stress

21-30: Medium stress

31-40: High stress

Stress score of the individual is assessed and recorded, to study is there any association between pre eclampsia and stress. stress level is reassessed in women with pre eclampsia .

Raddi sudha A, Randir Puri, Mc Metgud conducted a study to assess the level of stress and its manifestation in women with pre eclampsia. It was found that majority (64.61%) had moderate stress level. The association between level of stress and quality of life was studied and found quality of life was independent of level of stress.

SOCIOECONOMIC STATUS[18]

Gaurs socio economic classification is used to classify the socio economic status of subjects.

Class I	Upper class
Class II	Upper middle class
Class III	Lower middle class
Class IV	Upper lower class
Class V	Lower class

HUMAN CHORIONIC GONADOTROPIN- PREDICTOR OF PRE ECLAMPSIA

The human chorionic gonadotropin , a glycoprotein produced by syncytiotrophoblast cells of the placenta[34,35], is composed of two α and β subunits.It is detected in serum as early as in embryo with 8 cells and its important functions during pregnancy are implantation and decidualization, promotion of progesterone production, angiogenesis, differentiation of the cytotrophoblast and regulation of immune cells[4] .

Several variants of hCG have been characterized, the hyperglycosylated hCG (H-hCG) is a variant of hCG stimulating

trophoblastic invasion and is the major form of hCG during the first weeks of pregnancy[4,5].

Serum beta hCG peaks at 8 - 10 wk of pregnancy and then gradually declines, reaching a plateau level at 18 - 20 wk of pregnancy.

The free β-subunit can be derived from three sources, namely, direct production from trophoblast cell of placenta , dissociation of hCG into free α and β-subunits, and by neutrophils or macrophages enzymes nicking the hCG molecule[6].

The free β-hCG molecule that circulates in maternal serum will correspond to about 0.3-4% of the total hCG .

LEVELS OF b hCG DURING PREGNANCY

Weeks since LMP	B hCG level miu/ml
3 weeks	5-50
4 weeks	5-426
5 weeks	18- 7,340
6 weeks	1,080-56,500
7 -8 weeks	7,650-2,29,000
9-12 weeks	25,700-2,88,000
13- 16 weeks	13,300-2,54,000
17- 24 weeks	4,060- 1,65,400
25-40 weeks	3,640-1,17,000
Non pregnant Females	< 5
Post menopausal females	< 9.5

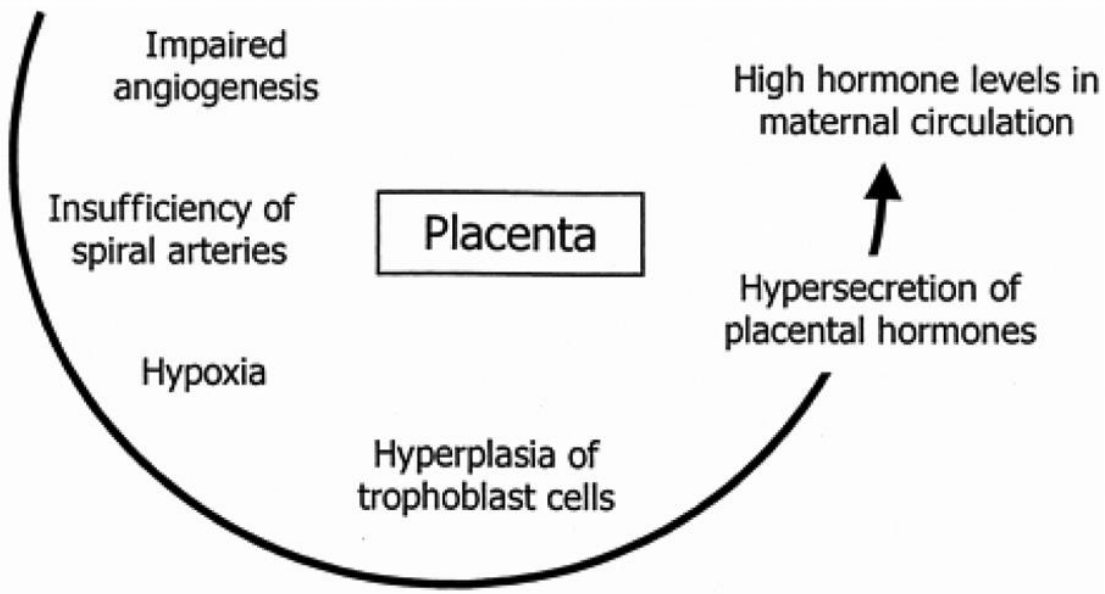
During pregnancy the normal placenta gets differentiated ,with the cytotrophoblastic cells dominantion in early pregnancy and the syncytotrophoblastic cells dominantion in late pregnancy[33].

In pre-eclampsia, focal cellular necrosis occurs in the syncytiotrophoblast and there is increased mitotic activity with proliferation of the cytotrophoblast [22,31] . In severe pre-eclampsia there is

rapid transformation of the proliferating trophoblast into syncytiotrophoblast[32].

The insufficient trophoblast migration into the spiral arteries and subsequent placental hypoxia results in elevated hCG production[36] by hyperplasic cytotrophoblastic cells of the placenta [9,23,24].

There is a relationship between pre -eclampsia and increased maternal serum β-HCG levels[25-30], which indicates that there is an abnormal secretary function of the placenta in patients with pre eclampsia[37].



Shows mechanism of elevated hCG in preeclampsia.

BETA hCG METHODOLOGY METHOD

Quantitative determination of beta hCG is done by Enzyme Immunoassay method[51].

There are two subunits in hCG named as alpha and beta. The molecular weight of b hCG is approximately 30,000 Daltons and its unique amino acid sequence confers to its biological and immunological specificity.

The molecular weight of alpha hCG is approximately 18,000 and it resembles to alpha sub unit of other glycoprotein hormones of pituitary namely thyroid stimulating hormone, luteinizing hormone and follicle stimulating hormone.

SAMPLE:

A venous blood sample is taken from the subjects and it is allowed to form clot and retract. After clot retraction the sample is centrifuged and clear serum is collected.

TEST PRINCIPLE:

- Microtitration wells are coated with specific monoclonal anti hCG antibodies.

- The test sera are applied with zero buffer and incubated
- If the sample contains human hCG it will combine with the antibodies on the well.
- Residual test specimen in the wells are washed and the wells are added with hCG antibodies labeled with Horseradish peroxide (HRP) enzyme.
- The hCG molecule gets sandwiched between the enzyme linked antibodies and the solid phase. The unbound labeled antibodies from the wells are washed after incubation.
- A colour will develop only in those wells that contain the enzyme after addition of the substrate(TMB).
- After stopping the reaction by adding dilute hydrochloric acid the absorbance is measured at 450 nm. The colour intensity of the test sample is directly proportionate to the concentration of hCG.

PROCEDURE:

* 50 microlitre of test serum are standards was dispensed into appropriate wells and then mixed gently for 30 seconds.

* 100 microliter of zero buffer was dispensed into each well and then mixed thoroughly for 10 seconds.

* Incubated at room temperature for 30 minutes.

* well contents discarded and washed five times with wash buffer.

* 150 microlitre of anti hCG HRP conjugate was added into each well and mixed for 5 seconds gently .

* Incubated at room temperature for 15 minutes .

* Well contents discarded and washed five times with wash buffer.

* 100 microlitre of substrate solution was added to each well and shaked for 5 seconds gently .

* Incubated for 20 minutes in dark at room temperature.

* 100 microlitre of stop solution was added to each well and shaked for 20 seconds gently .

* Optical densities was read immediately using a microplate reader with a 450 nm filter.

REVIEW OF LITERATURE

Hypertensive disorders complicates 5-10% of all pregnancies and it is the major cause (15-20%) 0f maternal mortality and of preterm births, intrauterine growth restriction, and perinatal mortality[19,20].

Preeclampsia is a multisystem disorder occurring after 20 weeks gestation that results in widespread vascular endothelial malfunction and vasospasm.

As early as 7 weeks gestation the normal physiological changes in pregnancy causes reduced vascular tone and low peripheral vascular resistance which reduces the maternal blood pressure.

At 16 -20 wks of gestation it reaches a nadir, and increases after 28 wks to reach the pre pregnancy level before term.

Early placental abnormalities point to the current hypotheses about the pathophysiologic mechanisms of the pregnancy induced hypertension. Throughout gestation the placenta synthesizes, steroid , protein and glycoprotein hormones[21].

For implantation and maintenance of the blastocyst the production of placental hCG is critical.

An association has been reported between second trimester levels of serum b hCG and pre eclampsia.

Worldwide maternal mortality(Khan and colleagues,2006) was systematically reviewed by the world health organization. 16% of maternal death were due to hypertensive disorder in developed countries which was greater than three other causes: haemorrhage accounting 13%, abortion and sepsis accounting 8% and 2% respectively.

Pre-eclampsia and eclampsia stand out as major causes of maternal and perinatal morbidity and mortality among the hypertensive disorders that complicate pregnancy . By timely and effective care to the women presenting with eclampsia and pre eclampsia, majority of deaths are avoidable with these complications.

Hypertension is defined by the International Society for the study of Hypertension in pregnancy (ISSHP) as, a blood pressure more than or equal to 140/90 mm Hg, recorded 4-6 hrs apart.

CLASSIFICATION:

The classification adopted by International society for the study of hypertension in pregnancy(ISSHP)[11] is

a. Gestational hypertension.

b. Preeclampsia - eclampsia

c. Chronic hypertension

- Essential
- Secondary

d. Superimposed preeclampsia on chronic hypertension.

- Gestational hypertension is defined as hypertension diagnosed after 20 weeks of gestation for the first time , without proteinuria .
- Transient hypertension : when the blood pressure becomes normal within 12 weeks of postpartum period.
- Chronic hypertension : hypertension persisting beyond 12 weeks after delivery.

- Preeclampsia :

Pre-eclampsia is defined as hypertension diagnosed after 20 weeks pregnancy associated with proteinuria;it is characterised by maternal response featuring systemic inflammation and variable degrees of placental dysfunction. Most consider hypertension and proteinuria to be the characteristic feature of preeclampsia, but the clinical manifestation of this syndrome are very heterogenous.

- Severe preeclampsia is characterised by one or more of the following features :

1. Severe hypertension (when blood pressure of 160/110 mmhg and above).
2. Proteinuria (5g/24 hours or 3+ or more in a random sample)
3. Oliguria (< 500 ml/ 24 hrs)
4. Pulmonary edema
5. Elevated serum creatinine
6. Microangiopathic hemolysis
7. Elevated ALT and AST

8. Thrombocytopenia (platelets < 1,00,000/ cu.mm)

9. Pain in the right upper quadrant or epigastrial pain

10. Intrauterine growth restriction

11. Features of end organ involvement (eg. visual disturbances or epigastric pain, headache.)

- Eclampsia is onset of seizures in cases of pre-eclampsia that cannot be attributed to any other cause.

- Superimposed pre-eclampsia on chronic hypertension

This term is defined as

- Newly onset proteinuria in women with hypertension alone in early weeks of gestation

- Hypertension and proteinuria in women prior to 20 weeks gestation exhibiting.

1. With sudden rise in blood pressure

2. Sudden increase in proteinuria

3. Thrombocytopenia

4. Elevated liver enzymes(AST, ALT)

- Chronic hypertension:

Chronic hypertension can be defined as presence of hypertension prior to pregnancy or hypertension which was diagnosed prior to 20 weeks gestation, but not due to gestational trophoblastic disease.Secondary hypertension may be caused by renal parenchymal disease, renovascular disease, endocrine disorders or aortic coarctation. Chronic hypertension is a strong risk factor for the development of pre-eclampsia.

EPIDEMIOLOGY

Pre-eclampsia constitutes a major cause of maternal and perinatal mortality and morbidity worldwide and in Western countries . It accounts about 3%–8% of pregnancy complication. Pre-eclampsia and eclampsia are directly associated with overall 10%–15% of maternal deaths. Some epidemiological data supports the hypothesis of an immunological and genetic etiology. With a maternal history of this disorder the risk for developing pre-eclampsia is 2-fold to 5-fold higher in pregnant women. Based on the ethnicity, the incidence of pre-eclampsia ranges from 1% to 3% among multiparas and 3% to 7% among healthy nulliparas.

Risk factors:

1. Extremes of maternal age at conception.

2. Multiple pregnancy

3. History of pre-eclampsia in previous pregnancy

4. Chronic hypertension and /or renal disease

5. Maternal chronic inflammatory conditions

6. Obesity

7. Pregestational diabetes mellitus

8. Maternal low birth weight

9. Smoking

10. Hydropic degeneration of the placenta

ETIOPATHOGENESIS

Pre-eclampsia seems to be a culmination of many factors that likely involve a number of placental, fetal and maternal factors. Those include:

1. Abnormal trophoblastic invasion of uterine vessels after placental implantation.
2. Maternal maladaptation to inflammatory or cardiovascular changes of normal pregnancy.
3. Immunological maladaptive tolerance between placental, fetal and maternal tissues.
4. Genetic factors.

The two basic abnormalities that are consistently seen are abnormal placentation and endothelial cell dysfuntion.

ABNORMAL PLACENTATION

The main organ involved in the syndrome of pre-eclampsia-eclampsia is essentially the placenta. Since pre eclampsia may occur in women with hydatidiform mole or an abnormal pregnancy, it indicates that uterine and fetal factors are not important in its pathogenesis.

Abnormalities in placentation resulting in lack of dilatation of the uterine spiral arteries leading to placental ischemia is the common underlying pathology in the genesis of pre-eclampsia.

In a normal pregnancy uterine spiral arterioles are invaded by trophoblasts. The endothelial lining and the muscular layer of the spiral arteries are disrupted and replaced by cytotrophoblasts converting the small calibre vessels into large capacity low resistance vascular spaces.

The process commences around 10-12 weeks and is completed by 18-20 weeks of pregnancy.

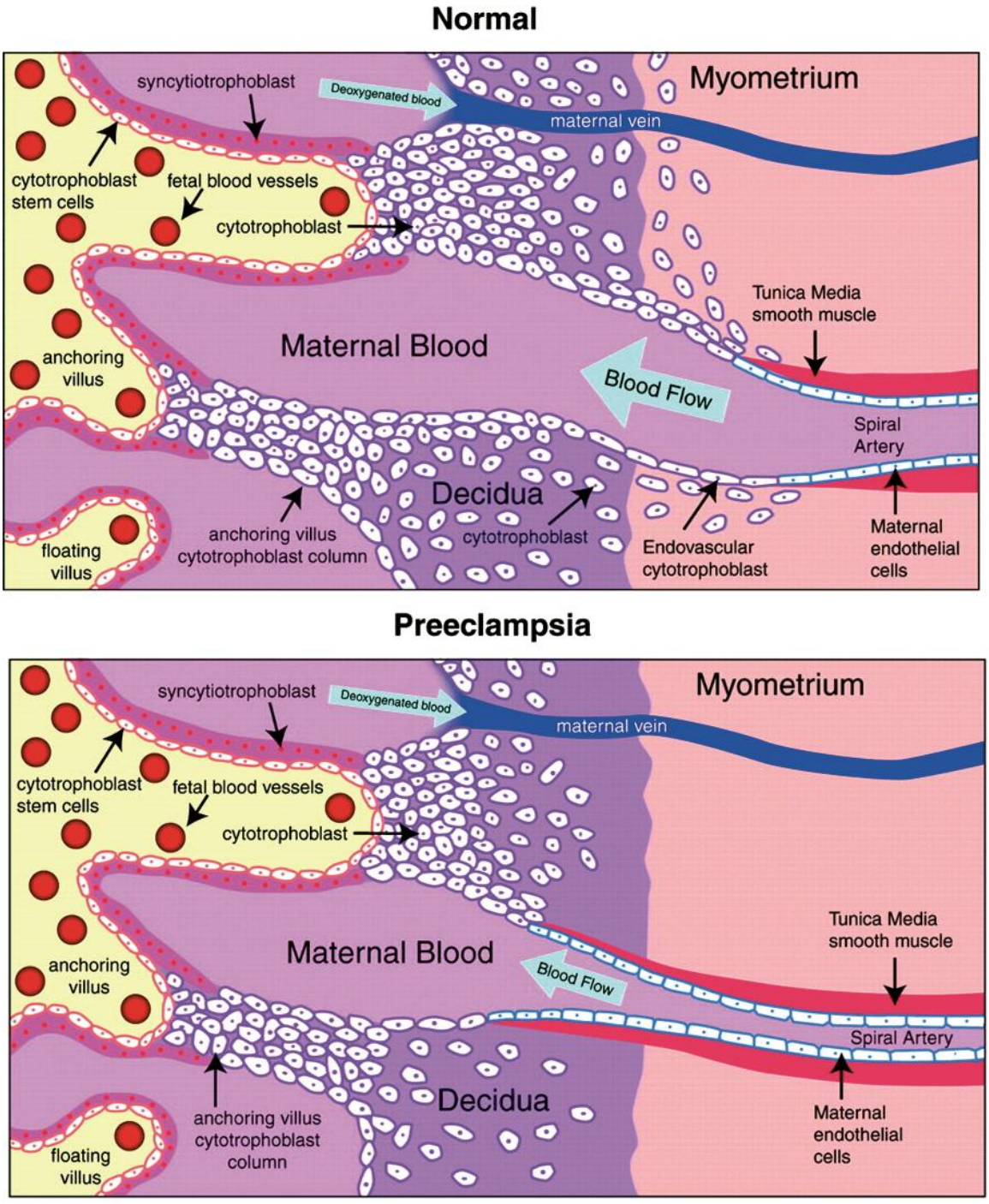
In pre-eclampsia the trophoblastic invasion is incomplete. Due to shallow invasion only the decidual vessels but not the myometrial vessels are lined with endovascular trophoblasts.

In deeper myometrial arterioles there is no loss of endothelial lining and musculoelastic tissue and their diameter is smaller than the normal placental vessels resulting in reduced uteroplacental flow.

Madazli and associates (2000) showed that the amount of defective trophoblastic invasion correlates with the severity of the disease.

The ensuing placental ischemia and hypoxia leads to an aberrant expression of genes encoding certain cytokines and vasoactive molecules

which contribute to the pathophysiology of pre-eclampsia. As a result, pro-inflammatory cytokines capable of eliciting endothelial dysfunction are released from the chorionic villi.



ENDOTHELIAL DYSFUNCTION

The central feature of pre eclampsia is endothelial cell dysfunction resulting in loss of vascular integrity, vascular reactivity and activation of coagulation cascade.

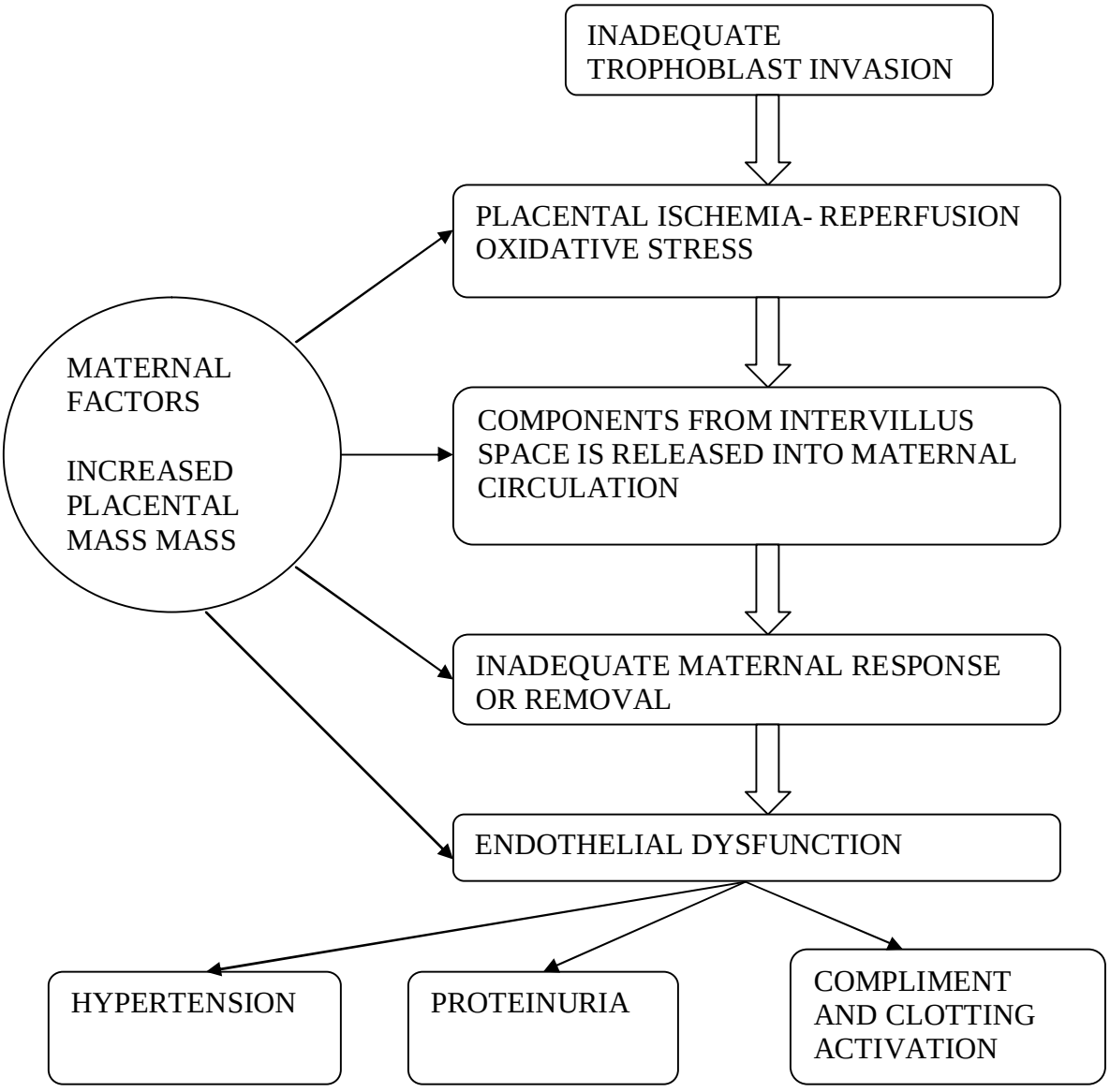
Endothelial dysfunction is due to extremely activated luekocytes secreting cytokines like tumor necrosing factor -α and interleukins which causes production of reactive oxygen materials and free radicals that leads to formation of lipid peroxides causing endothelial injury.

Other effects of oxidative stress includes production of lipid laden macrophages seen in atherosis and activation of microvascular coagulation . It manifests as thrombocytopenia and increased capillary permeability causing edema and proteinuria.

Intact endothelium has anticoagulant properties, but damaged or activated endothelium of the vessel wall triggers platelet aggregation , and changes in the production of various coagulation factors resulting in increased thrombin and fibrin formation.

Both coagulation and fibrinolytic activity is increased in normal pregnancy but the coagulant activity is further enhanced in pre eclampsia.

PATHOPHYSIOLOGY OF PRE-ECLAMPSIA



IMMUNOLOGICAL FACTORS

Loss of maternal immune tolerance or its dysregulation to paternally derived placental and fetal antigens is another theory for pre eclampsia.

Redman and colleagues (2009) recently reviewed role of immune maladaptation in the pathophysiology of pre eclampsia. In pre eclampsia trophoblasts express reduced amounts of immuno-suppressive human leucocyte antigen -G (HLA-G) leading to defective vascularisation .

GENETIC FACTORS

Pre-eclampsia is a multi factorial , polygenic disorder.

The incident risk for pre-eclampsia for daughters of pre-eclamptic mothers is 20 to 40 %, 22 to 47% in twins and 11 to 37% for sisters as cited by Ward and Lindheimer (2009).

PATHOGENESIS

Vasospasm :

This concept was advanced by Volhard in 1918. Vascular constriction causes increased resistance and hypertension. Endothelial cell damage causes interstitial leakage. The platelets and fibrinogen are

deposited subendothelially. Due to reduced blood flow and its maldistribution there is ischemia of the tissues resulting in hemorrhage, necrosis and end organ damage characteristic of the syndrome.

Increased pressor responses :

In pregnancy normally there is refractoriness to vasopressors but in pre eclampsia there is increased vascular reactivity to the infused vasopressors (norepinephrine, angiotensin II).

Prostaglandins :

Endothelial production of prostacyclin is decreased in pre eclampsia and this is mediated by phospholipase A2. Thromboxane A2 secretion by platelet is increased and the prostacyclin : thromboxane ratio decreases. the net result favours increased sensitivity to infused angiotensin and ultimately vasoconstriction.

Nitric oxide :

Nitric oxide is a potent vasodilator which is synthesised from L-arginine by endothelial cells .In fetoplacental unit , nitric oxide maintains the low pressure vasodilated state increasing the perfusion. In pre eclampsia there is decreased expression of nitric oxide synthase and increased nitric oxide deactivation.

Endothelins:

This is a potent vasoconstrictor. Human endothelium produces endothelin -1 which is the primary isoform. In pregnancy plasma ET -1 level is increased but even more increased in pre eclampsia.

Angiogenic and anti angiogenic proteins :

There exists an angiogenic imbalance between these two proteins , excess amount of antiangiogenic factors are hypothesised to be stimulated by hypoxia in the uteroplacental interface. Two anti angiogenic proteins (soluble Fms - like tyrosine kinase and soluble endoglin) are overproduced by trophoblastic tissues in women destined to develop pre eclampsia.

Maternal susceptibility:

1.Maternal susceptibility genes

Preeclampsia is a multifactorial , polygenic disorder.The incident risk for preeclampsia for daughters of pre-eclamptic mothers is 20 to 40 %, 22 to 47% in twins and 11 to 37% for sisters as cited by Ward and Lindheimer (2009).

2. Thrombophilias

Initial studies showed clear association between early onset pre eclampsia and maternal thrombophilias. In a two hit type model of pre eclampsia the triggering factor is exacerbated by some other factors, thrombophilia is one such exacerbating factor pr second hit.

Age :

Extremes of age are risk factors of pre eclampsia. Among teenagers the high risk of pre eclampsia is most likely due to short period of sperm exposure. In advanced maternal age it is due to the combined effect of ageing endothelium and other adverse factors like increased booking BP and BMI.

Chronic hypertension :

High BP at booking visit is a major risk factor for pre eclampsia.

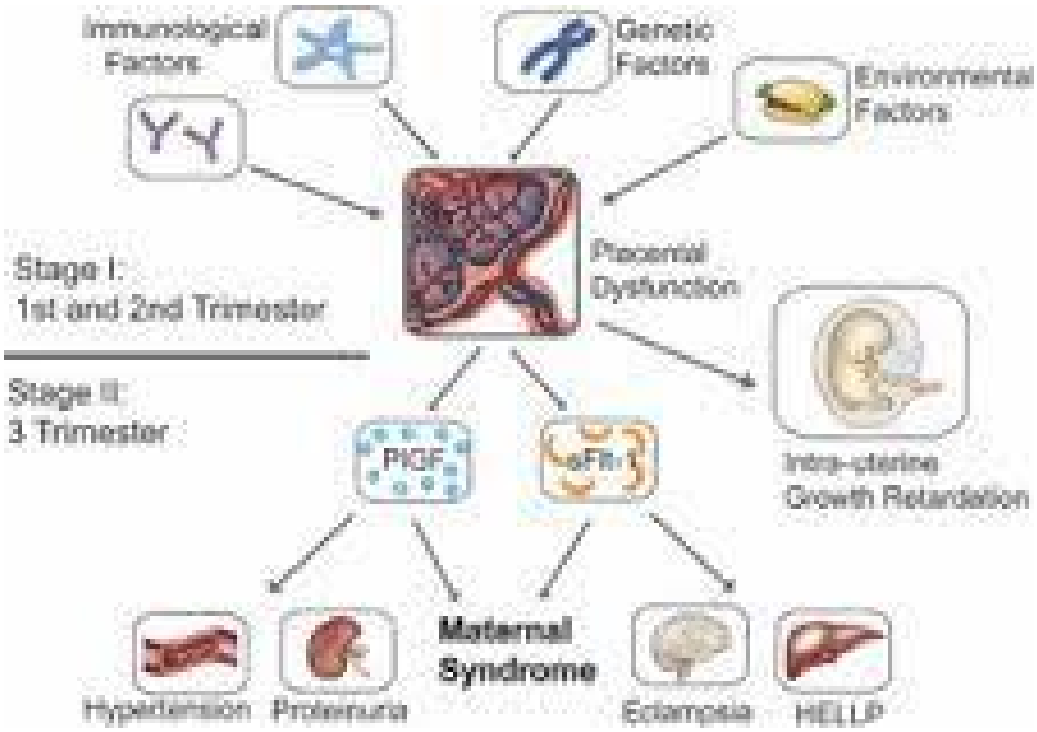
Obesity:

Obesity is a risk factor for both pre eclampsia and gestational hypertension. Risk doubles with every 5-7 kg/ m^2 increase in pre pregnancy BMI.

PATHOPHYSIOLOGY

As a consequence of vasospasm, endothelial dysfunction and ischemia pre eclampsia results in multi organ involvement with a clinical spectrum ranging from barely noticeable to severe pathophysiological deterioration which may be life threatening to both fetus and mother.

ETIOLOGY AND EFFECTS OF PREECLAMPSIA



Cardiovascular system:

Cardiovascular changes seen in pre eclampsia is due to

1. Increased afterload caused by hypertension;
2. Cardiac preload , which is affected by diminished hypervolemia of pregnancy or iatrogenically increased by oncotic solutions or intravenous cystalloids;
3. Endothelial activation with extravasation of fluid from intravascular to extracellular space.

Hemodynamic changes:

The cardiovascular aberrations of pregnancy related hypertensive disorders center around increased afterload and severity of hypertension , presence of pre eclampsia , presence of any chronic disease and stage of clinical course during which they are studied.

Hemoconcentration is a hallmark of pre eclampsia, it results from generalized vasoconstriction that follows endothelial activation and due to leakage of plasma to interstitial space.

BLOOD AND COAGULATION

Thrombocytopenia

The frequency and intensity of thrombocytopenia depends on the duration and severity of the pre-eclampsia. Overt thrombocytopenia is defined as platelet count < 1,00,000 per cu mm. and it indicates severe disease. After delivery platelet count may continue to fall for the first day or so, then progressively increases to reach normal level within 3-5 days.

Hemolysis

Hemolysis is the evidence of severe pre-eclampsia which is quantified by the level of serum lactate dehydrogenase and other evidences in peripheral blood are schizocytosis, spherocytosis, and reticulocytosis. These derangements result partly from microangiopathic hemolysis caused by endothelial disruption, platelet adherence and deposition of fibrin. Erythrocyte membrane changes , increased aggregation and adhesiveness may facilitate hypercoagulable state .

HELLP Syndrome

This is characterised by hemolysis, thrombocytopenia and elevated serum liver transaminase levels, commonly found in severe pre-eclampsia and it is indicative of hepatocellular necrosis.

Coagulation

The changes consistent with intravascular coagulation and red cell destruction are found in preeclampsia and eclampsia. There is increased consumption of factor VIII ,increased fibrinopeptide A and B levels and increased fibrin degradation products , and decreased levels of antithrombin and protein C and S. Except for thrombocytopenia other coagulation aberrations are generally mild.

Kidney:

There occur several reversible structural and pathophysiological changes in kidneys in case of pre-eclampsia.

The diminished glomerular filtration rate may results from reduced plasma volume , increased renal afferent arteriolar resistance and glomerular endotheliosis blocking the filtration barrier. Due to diminished filtration rate serum creatinine value rises to values seen in non pregnant women that is 1 mg/dl and sometimes even higher.

Plasma uric acid elevation is typically seen in pre eclampsia this is likely to be due to enhanced tubular reabsorption. Pre-eclampsia is associated with diminished urinary calcium excretion because of increased tubular reabsorption.

Proteinuria:

Proteinuria is defined as 24 hours urinary protein excretion greater than 300 mg or persistent 30mg/ dl protein(1+dipstick) , or a urine protein : creatinine ratio $\geq$ 0.3 in a random urine sample.

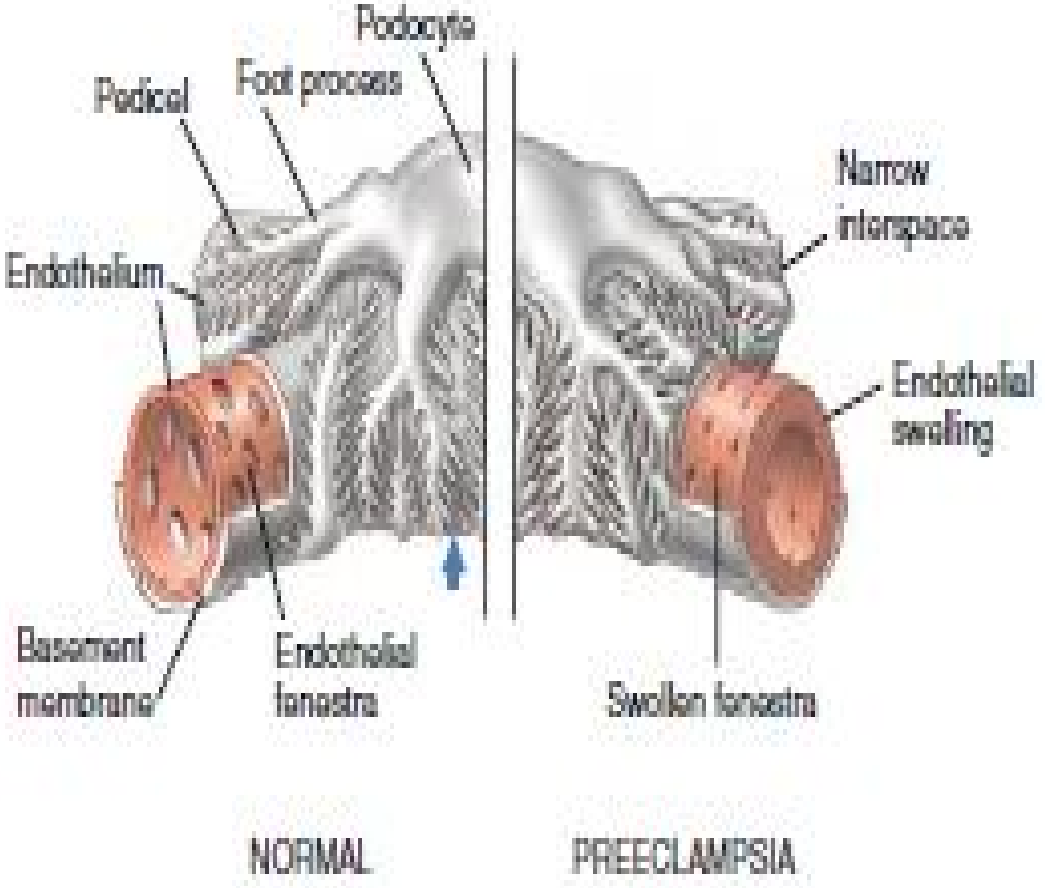
Anatomical changes

Glomerular endotheliosis is characteristic of pre-eclampsia. Glomeruli are enlarged by 20%, they are bloodless and capillary loops are dilated and contracted variably.

Endothelial cells are swollen that they block the capillary lumens and homogenous subendothelial deposits of proteins and fibrin like materials are also seen.

There is evidence that the endothelial swelling is due to angiogenic factor withdrawal (Karumanchi and colleagues, 2009). Angiogenic protein is important for podocyte health , its inactivation by antiangiogenic receptors leads to dysfunction of podocytes and swelling of the endothelium.

Glomerular Changes in Pre Eclampsia



Acute renal failure

Acute tubular necrosis caused by pre-eclampsia alone is rare, clinically detectable renal failure is induced by the coexistent hemorrhagic hypotension invariably.

Liver

Periportal hemorrhage in the periphery of the liver is the common characteristic lesion found. Liver involvement in pre-eclampsia is clinically evident in following situations

1. Symptomatic involvement of liver - Right upper quadrant pain or mid epigastric pain and tenderness in the right hypochondrium seen in severe disease.

2. Asymptomatic elevation of liver enzymes, SGOT and SGPT are considered as markers of severe pre eclampsia. Values rarely exceeds 500U/L,but in some cases it has been reported to exceed 2000U/L. Generally serum levels of liver enzymes follow the platelet levels inversely, and both gets normalized within three days of delivery.

3. Hepatic hematoma can be formed due to extension of hepatic hemorrhage from the areas of infarction. This in turn can extend and form subcapsular hematoma that may rupture.

Unruptured hematomas are common than clinically suspected and they are more likely associated with HELLP syndrome.

BRAIN

Brain involvement accounts for about only one third of fatal cases.

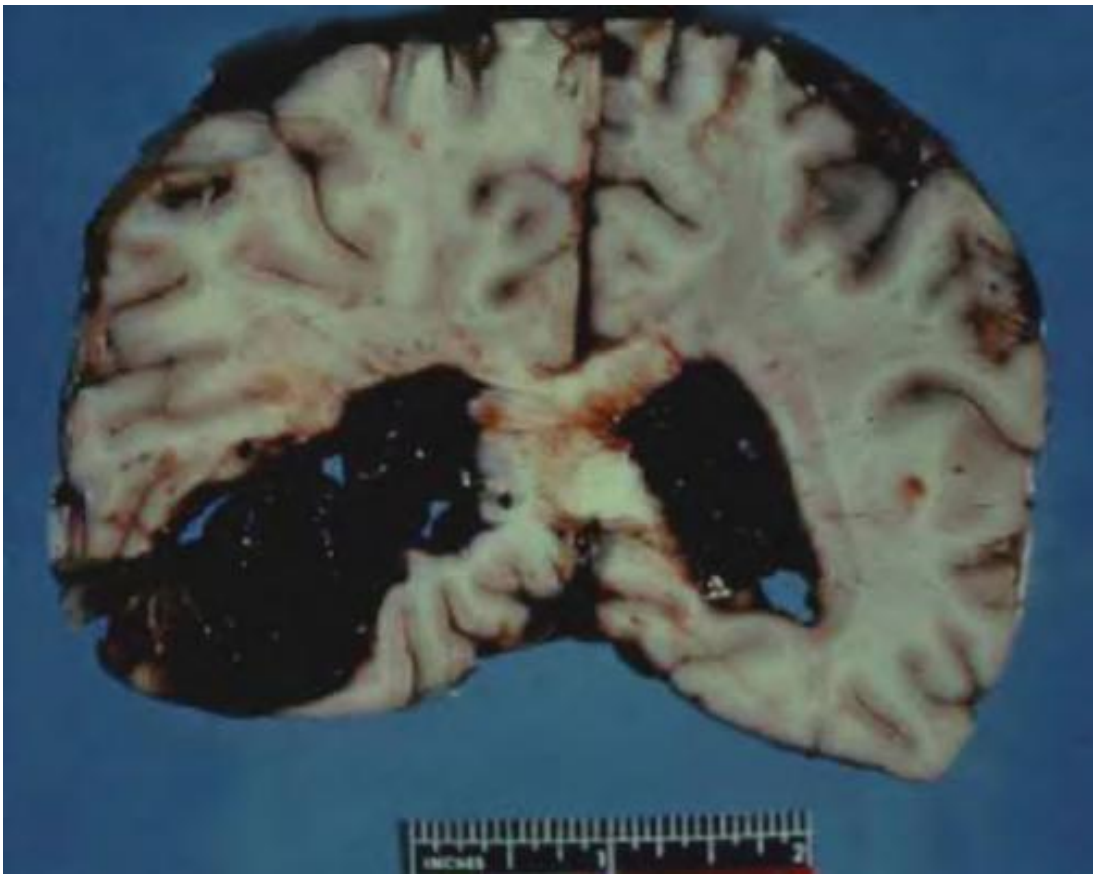
Most maternal deaths were due to pulmonary edema and brain pathology were coincidental.

Although gross intracerebral hemorrhage were seen in about 60% of eclampsia patients, it was fatal in only half of them.

Other lesions found were cortical and subcortical petechial hemorrhage , subcortical edema, hemorrhage in white matter and in basal ganglia or in pons . Many non hemorrhagic areas of softening seen throughout brain.

The classical microscopic lesion consists of fibrinoid necrosis of arterial wall, perivascular microinfarcts and hemorrhages.

Fatal hypertensive hemorrhage in a primigravid woman with eclampsia



There are two general theories to explain the cerebral abnormalities

1. The first theory suggests that acute and severe hypertension causes vasospasm , diminished cerebral blood flow resulting in ischemic changes, cytotoxic edema and brain tissue infarction.

2. The second theory is that sudden increase in blood pressure exceeds the autoregulatory capacity of cerebrovascular system and causes disruption of the pressure in the end capillaries thereby causing increased hydrostatic pressure, increased vascular permeability, and extravasation of plasma leading to vasogenic edema.

Thus, pre-eclampsia syndrome has endothelial activation associated with interendothelial leak causing vasogenic edema . this is referred as posterior reversible encephalopathy syndrome.

Clinical manifestations

1. Headache and scotomata could be due to cerebrovascular hyperperfusion commonly involving the occipital lobes. The headache may be mild or severe pain and may be intermittent or constant in nature . Usually these symptoms will improve after initiating magnesium sulfate infusion.

2. Convulsion are diagnostic of eclampsia.

3. Generalised cerebral edema may develop, usually manifests as altered sensorium that vary from confusion to coma.

Visual changes

Scotomata ,blurring of vision or diplopia are commonly seen in severe preeclampsia and eclampsia.

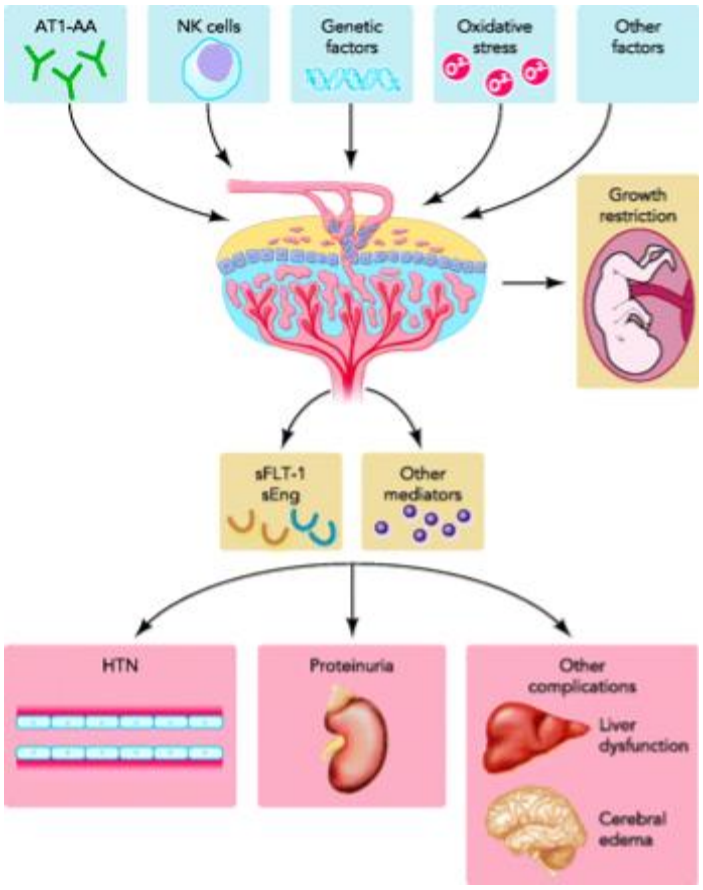
Blindness may arise from three areas- visual cortex in occipital lobe, retina and lateral geniculate nuclei.

Occipital blindness also called amaurosis , usually the affected person have evidence of vasogenic edema in occipital lobe on imaging studies.

Blindness caused by retinal lesions like retinal ischemia or infarction is called purtscher retinopathy.

Retinal detachment ,may also cause loss of vision .Usually it is unilateral and rarely causes complete loss of vision.

PATHOGENESIS OF PREECLAMPSIA



Maternal complications of pre eclampsia- eclampsia[12,13]

1. Eclampsia- is defined as the development of seizures and / or unexplained coma in women with symptoms and signs of pre eclampsia, during pregnancy or in postpartum period.

2. Cerebrovascular accidents

3. Abruptio placenta

4. HELLP syndrome (Hemolytic anemia, elevated liver enzymes , low platelets)

5. Acute left ventricular failure with pulmonary edema

6. Acute renal failure

7. Microangipathic hemolytic anemia

Fetal complications

1. Intrauterine death

2. Intrauterine growth restriction

3. Pre maturity and its associated hazards

4. Ante partum and intra partum asphyxia

PREDICTION AND PREVENTION

Measurement of various biochemical, biological and biophysical markers in early pregnancy or across the pregnancy has been proposed to predict the development of pre-eclampsia. Currently there are no screening tests for early prediction that are reliable, economic and valid.

PLACENTAL PERFUSION / VASCULAR RESISTANCE TESTS

Provocative pressor tests :

1. Roll over test : Measures the hypertensive response in women who are resting in left lateral position and then roll over to supine position. test is done at 28- 32 weeks. Gant et al reported that when there is rise in diastolic pressure by 20 mmhg or more within 5 minutes after changing from left lateral to supine position.

2. Isometric exercise test :

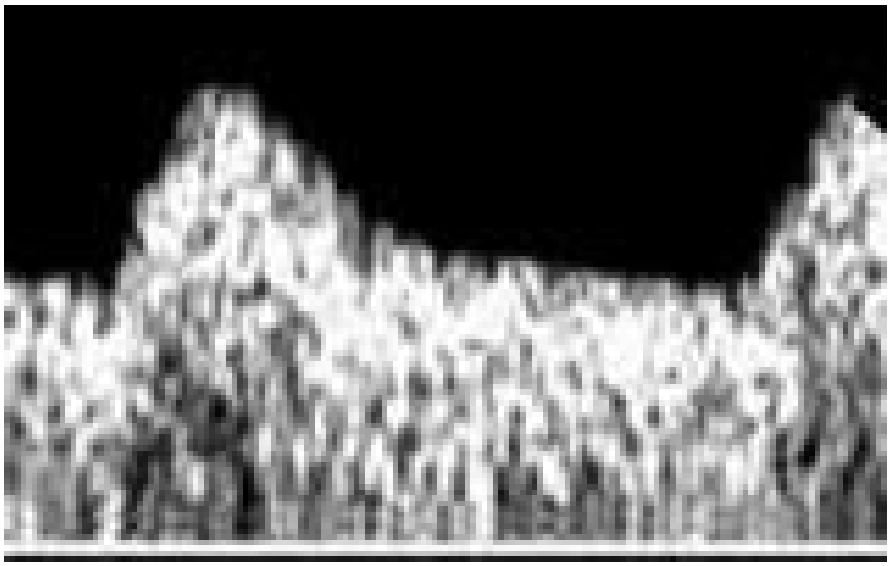
   It applies the same principle by squeezing the handball.

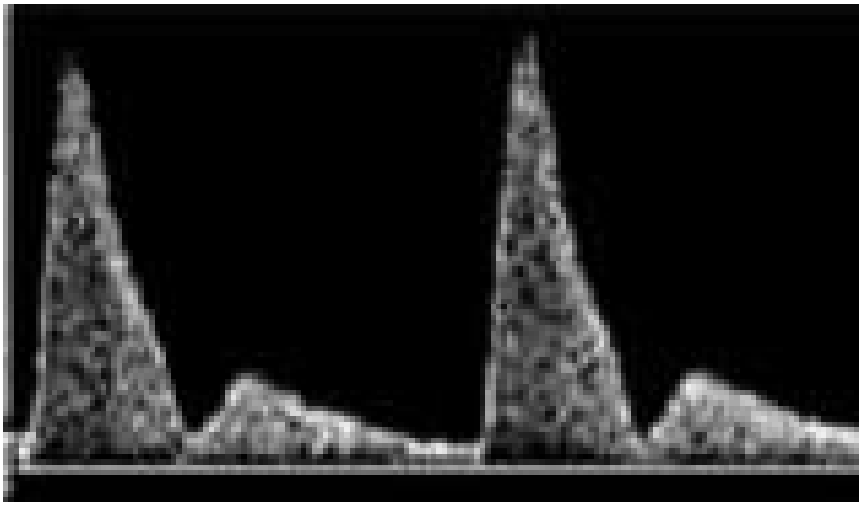
3. Angiotensin II infusion test:

This test is based on the loss of refractoriness to angiotensin ,it is performed by giving incremental increasing dose of angiotensin intravenously. In normal pregnancy, the women requires mean angiotensin II doses of 13.5 to 14.9 ng/kg/minute to rise the diastolic blood pressure by 20 mm Hg.

Uterine artery doppler velocitometry:

Abnormal trophoblastic invasion of spiral arteries results in diminished placental perfusion and increased uterine artery resistance. It is seen in doppler ultrasound as abnormal waveform represented by increased diastolic notch.





Uterine artery Doppler without and with a notch.

RENAL DYSFUNCTION -RELATED TESTS

Serum uric acid :

Hyperuricemia is one of the earliest laboratory manifestations. It results from diminished glomerular filtration, reduced uric acid clearance, increased tubular reabsorption and decreased secretion.

Microalbuminuria :

Conde-Agudelo and associates (2009), reported that this test has sensitivity of about 7 to 90 percent and specificity of about 29% to 97 %.

BIOCHEMICAL MARKERS

Several biochemical predictors describe the fetal and placental endocrine functions and the maternal endothelial dysfunction.

Placental protein

Placental protein 13 (PP 13), secreted by syncytiotrophoblasts, has been found to be at a lower level in first trimester in women who developed early-onset pre-eclampsia later when compared to women without preeclampsia. Abnormal trophoblastic invasion also causes reduced amount of placenta derived proteins, pregnancy-associated protein A (PAPP-A) in women prone for pre-eclampsia[8].

Alfa fetoprotein (AFP)

The failure of trophoblast invasion causes alteration of the surface layer of the syncytiotrophoblasts resulting in leakage of alfa fetoprotein (AFP) and its increased level in the maternal circulation[7].

Inhibin A and Activin A

They belong to transforming growth factor β super family and both were found to be elevated before the onset of pre-eclampsia.

Fibronectins:

This is a high molecular weight glycoprotein released from endothelial cells and extracellular matrix following injury to endothelium. Stubbs and colleagues that plasma concentration of fibronectin is increased in pre-eclampsia. Leefang and associates(2007) reported that neither total fibronectin nor cellular level was useful to predict pre-eclampsia.

Angiogenic factors:

Serum levels of pro-angiogenic factors like vascular endothelial growth factors (VEGF) and placental growth factor (PlGF) are decreased before preeclampsia develops. Anti-angiogenic factors like soluble fms -

like tyrosine kinase 1 and soluble endoglin are increased. Measurement of their plasma levels may predict the pre-eclampsia.

Free Fetal DNA

DiFederico and colleagues in 1999 , hypothesized that accelerated apoptosis of cytotrophoblasts results in release of free DNA. Using polymerase chain reaction , free fetal DNA in maternal plasma can be detected.

PREVENTION OF PRE-ECLAMPSIA

Diet And Exercise

Weight control might lower the risk of pre-eclampsia . There are no randomized studies to prove this benefit.

Periconceptional and first trimester vitamin B12 and folate might reduce the risks not only for neural tube defects but also for pre-eclampsia.

A systematic review of supplementation of calcium in preventing pre-eclampsia found reduction in risk by 30%.

Aspirin and anti-platelet drugs

Starting low dose aspirin early in the second trimester offers some benefit for a women who were at high risk of developing early onset pre-eclampsia. In a systematic review of 43 trials low dose aspirin and anti platelet drugs were found to reduce the risk by 19%.

- Gurmandeep kaur, vimla Jain, Seema Mehta and Sunita Himani tested the hypothesis that women with elevated serum beta-hCG in early gestation are at higher risk of developing pre-eclampsia. Serum β HCG estimation was done at 13-20 weeks of gestation by CLIA method in 200 women and they were followed till delivery for development of pre eclampsia.

Out of 200 women ,178 were evaluated finally . Of whom 22 developed pre-eclampsia. Beta HCG levels > 2 multiple of median were considered raised. Out of 24 women with beta HCG > 2 MOM 22 developed pre-eclampsia against 2 women developed PIH out of 154 with beta HCG < 2 MOM.

Study concluded that estimation of serum β hCG at mid trimester is a good predictor for pre-eclampsia and higher levels are associated with increased severity of pre-eclampsia (P value < 0.01). The sensitivity was

90.91 %, specificity was 97.44 % and positive predictive value was 83.33 %.

- Remzi Gokdeniz, Erdal Ariguloglu, Nursel Bazoglu, Ozcan Balat conducted a study at department of obstetrics and gynecology, Faculty of Medicine,Inonu university, Malatya-turkey, to determine whether serum hCG levels reflects a different secretory response of trophoblasts in pre-eclampsia. Thirteen severe pre-eclampsia women were matched against twenty one pregnant normotensives with singleton pregnancy in third trimester.

Severe pre-eclampsia patients found to have significantly higher beta hCG levels compared with controls ($p < 0.05$).

There was no difference between two groups in view of mean age, age of gestation or serum creatinine value ($p > 0.05$). In pre-eclampsia group, mean arterial pressure, serum uric acid and beta hCG were significantly higher than the control group ($p < 0.05$).

In conclusion there is a strong relationship between elevated serum beta hCG and severe pre-eclampsia.

- Dayal Meena ,Gupta Parul, Varma Manju, Ghosh UK, Bhargava Anudita conducted a study to evaluate the clinical use of second trimester serum markers as a predictor of pre-eclampsia.

It is a prospective study done by estimating the levels of β HCG , α feto protein and inhibin A in 50 antenatal women in second trimester (12-24 weeks) by ELISA method.

Out of 50 , 10 women developed pre-eclampsia (20%) . A significant rise in β HCG (>2.5 MOM,16130.2 miu / ml,$p < 0.001$), mean serum α feto protein level (> 2.5 MoM, 161.7 ng/ml, $p < 0.001$),and the mean inhibin A (>2.0 MoM, 1248.49 pg/ml, $p < 0.001$) was present in women who developed pre-eclampsia.

In conclusion there exists a significant positive correlation between elevated serum markers in second trimester and development of pre-eclampsia $p < 0.001$.

Vidyavathi RK, Hijam Davina, et al. (2010) measured β hCG level and serum lipid profile between 14 and 20 weeks of gestation. β hCG levels and triglycerides, VLDL, LDL and total cholesterol are raised in those who developed PIH. Study suggested that β hCG level and lipid profile are effective predictors of PIH.

- Sorensen TK, Williams MA, et al (1993) measured serum hCG levels in second trimester and followed up the cases for the development of PIH, which suggested second trimester hCG level can be a potential marker for pregnancy induced hypertension.

- Gonen R, Perez R, David M, Dar H, (1992) conducted the study which measured hCG at second trimester, which showed the risk of hypertension among women with elevated hCG was high .

- Said ME, Campbell DM, Azzam ME, et al (1984) measured beta hCG serially during pregnancy, which showed that beta hCG was found to rise before clinical signs of preeclampsia appeared.

MANAGEMENT OF MILD PRE ECLAMPSIA

If significant hypertension and albuminuria is detected, the patient may be hospitalized to evaluate her and the fetus.

* Rest: Advised bed rest throughout the greater part of day and night. Lying in left lateral position improve the uterine blood flow and help in fetal growth.

* Diet: Salt restriction is not necessary and encourage to eat a normal diet.

* Diuretics: Diuretics are harmful and are indicated only in pulmonary edema or heart failure.

* Monitoring of the mother: Monitor blood pressure twice daily and examine urine daily for albuminuria.

* Monitoring of the fetus: Fetal well being is ascertained by fetal movement count. Fetal growth is assessed clinically and sonologically.

* Gestation less than 37 weeks: If the diastolic blood pressure settles and proteinuria becomes insignificant, the patient shall be discharged with the advise of bed rest and regular blood pressure check up.

* Gestation more than 37 weeks: Labour is induced if there is any fetal compromise. If there is no fetal compromise and the pre eclampsia does not worsen, pregnancy shall be continued for another week.

MANAGEMENT OF SEVERE PRE ECLAMPSIA

All patient with severe pre eclampsia must be hospitalized and advised bed rest and diet as in mild pre eclampsia.

Antihypertensive therapy: The goal is to keep the diastolic BP between 90 and 100. However, anti hypertensive drugs have not been helpful in improving the perinatal outcome.

Drugs: Recently labetalol (starting dose 100 mg BD, maximum dose 2.4 gm/day) is recommended as the best drug in pre eclampsia to control BP. Methyl dopa, initially in a dose of 250 mg three times daily and later increased to 4gm/day. Intra venous labetalol is useful in quick control of hypertension in severe pre eclampsia.

RESPONSE TO TREATMENT

If the maternal condition improves and no evidence of imminent eclampsia or fetal compromise, the pregnancy shall be continued until 36 or 37 weeks, under strict vigilance. On the other hand if maternal condition worsens or if symptoms of imminent eclampsia develops, the pregnancy must be terminated, irrespective of the period of gestation.

Severe pre eclampsia by itself is not an indication of cesarean section. Prophylactic magnesium sulfate should be given in patient with severe pre eclampsia.

RESULTS AND DISCUSSION

The study group was grouped into two, depending upon the development of pre-eclampsia, as normal cohort and pre-eclamptic cohort

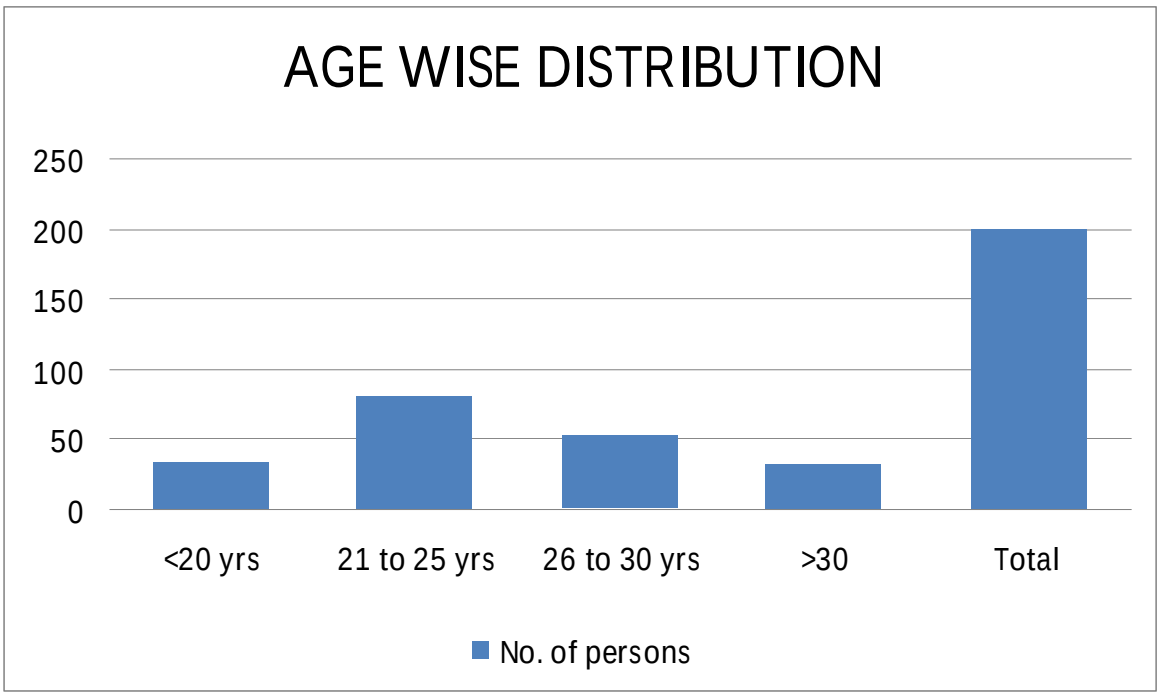
The variables that are considered in this study are, age group, obstetric score, socio economic class, pre pregnancy weight, body mass index, stress score, beta human chorionic gonadotrophin value. For each variable Mean +SD of all variables of interest were determined for pre-eclampsia cohort and for normal cohort separately and difference was tested by chi-square test.

The predictive values of beta human chorionic gonadotrophin was analyzed using pearson’s ROC curve. Comparison of variables was done using chi-square test.

AGE WISE DISTRIBUTION

Age	No. of persons	%
<20 yrs	34	17
21 to 25 yrs	81	40.5
26 to 30 yrs	53	26.5
>30	32	16
Total	200	100

Table No: 1

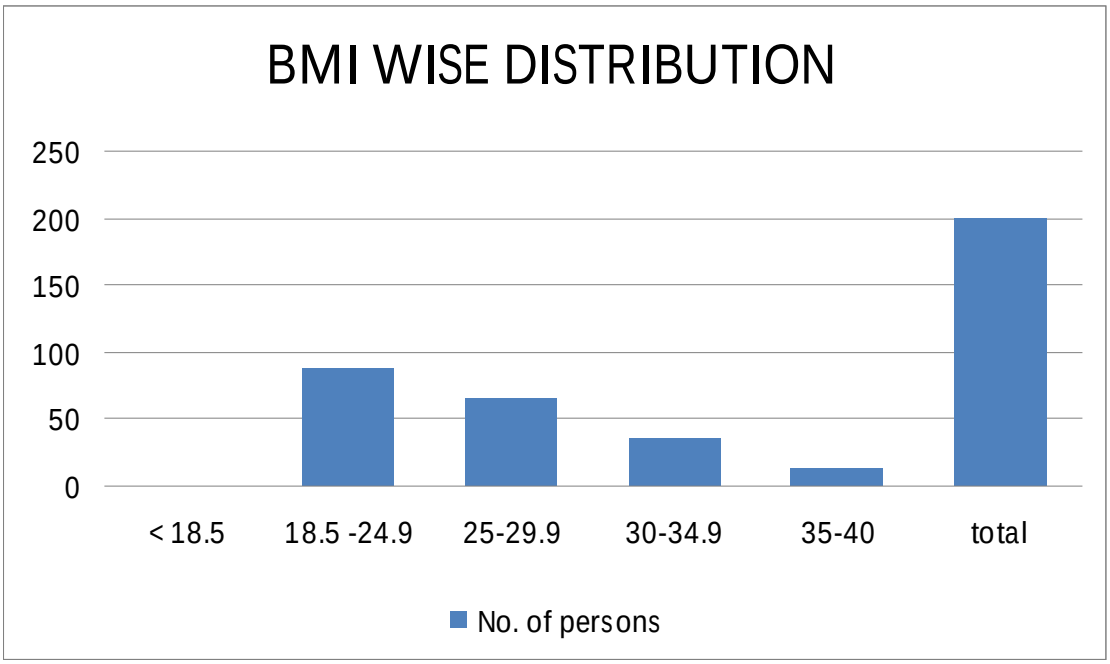


Majority(40.5%) of study subjects were in the age group between 21 and 25. 16% of subjects were above 30 years and 17% were below 20 yrs of age.

BMI WISE DISTRIBUTION

BMI	No. of persons	%
< 18.5	0	0
18.5 -24.9	88	44
25-29.9	65	32.5
30-34.9	35	17.5
35-40	12	6
total	200	100

Table No:2



As per the WHO classification of obesity the majority (44%) of the study subjects were in the BMI(Body Mass Index) between 18.5 and 24.9(healthy weight). 32.5% were over weight by BMI. 17.5% of subjects were moderate obese and only 6% were severe obese.

SOCIO ECONOMIC STATUS WISE DISTRIBUTION

Socio economic status	No. of persons	%
class 2	4	2
class4	60	30
class5	136	68
Total	200	100

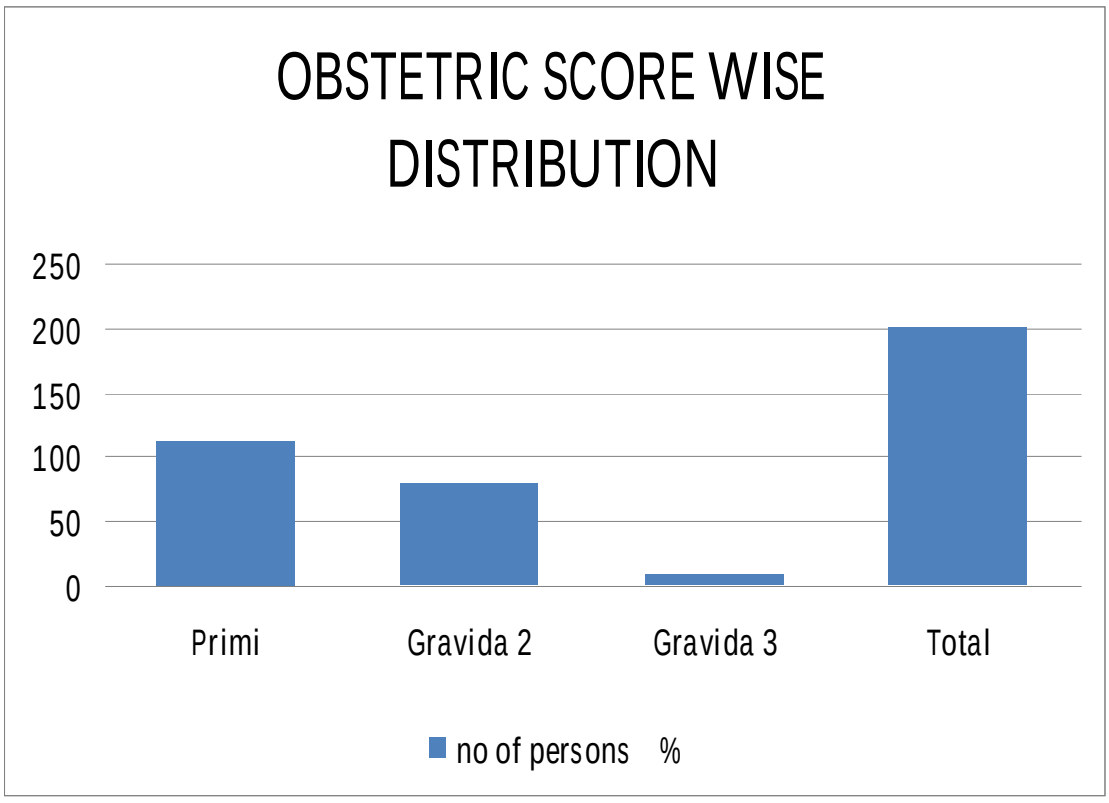
Table No:3

As per Gaurs socio economic classification, majority(68%) of study subjects belong to class 5(lower class) and 30% belong to class 4(upper lower class). Only 2% of study subjects belong to class2(upper middle class).

OBSTETRIC SCORE WISE DISTRIBUTION

Obstetric score	no of persons	%
Primi	112	56
Gravida 2	80	40
Gravida 3	8	4
Total	200	100

Table No:4



56% of study subjects were primi and 40% were gravida 2. Only 4% of study subjects belong to gravida 3 category.

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
AGE GROUP * PREECLAMPSIA	200	100.0%	0	.0%	200	100.0%
PARITY * PREECLAMPSIA	200	100.0%	0	.0%	200	100.0%
GDM * PREECLAMPSIA	200	100.0%	0	.0%	200	100.0%
URINE ALBUMIN * PREECLAMPSIA	200	100.0%	0	.0%	200	100.0%
SOCIOECONOMIC CLASS * PREECLAMPSIA	200	100.0%	0	.0%	200	100.0%

Table no 5

AGE GROUP - OCCURRENCE OF PREECLAMPSIA					
			PREECLAMPSIA		
			0	1	Total
AGE GROUP	1	Count	18	16	34
		% within PREECLAMPSIA	11.5%	36.4%	17.0%
		% of Total	9.0%	8.0%	17.0%
	2	Count	73	8	81
		% within PREECLAMPSIA	46.8%	18.2%	40.5%
		% of Total	36.5%	4.0%	40.5%
	3	Count	45	8	53
		% within PREECLAMPSIA	28.8%	18.2%	26.5%
		% of Total	22.5%	4.0%	26.5%
	4	Count	20	12	32
		% within PREECLAMPSIA	12.8%	27.3%	16.0%
		% of Total	10.0%	6.0%	16.0%
	Total	Count	156	44	200
		% within PREECLAMPSIA	100.0%	100.0%	100.0%
		% of Total	78.0%	22.0%	100.0%

Table no 6

Chi square value - 25.333 p value - 0.000, which is significant

OCCURENCE OF PRE ECLAMPSIA AMONG VARIOUS AGE GROUP

Age Group (yrs)	Pre-eclampsia cohort		Normal cohort	
	No of Cases	%	No of Cases	%
< 20	16	36.4 %	18	11.5 %
21 - 25	8	18.2 %	73	46.8 %
26 - 30	8	18.2 %	45	28.8 %
> 30	12	27.3 %	20	12.8 %

Table no 7

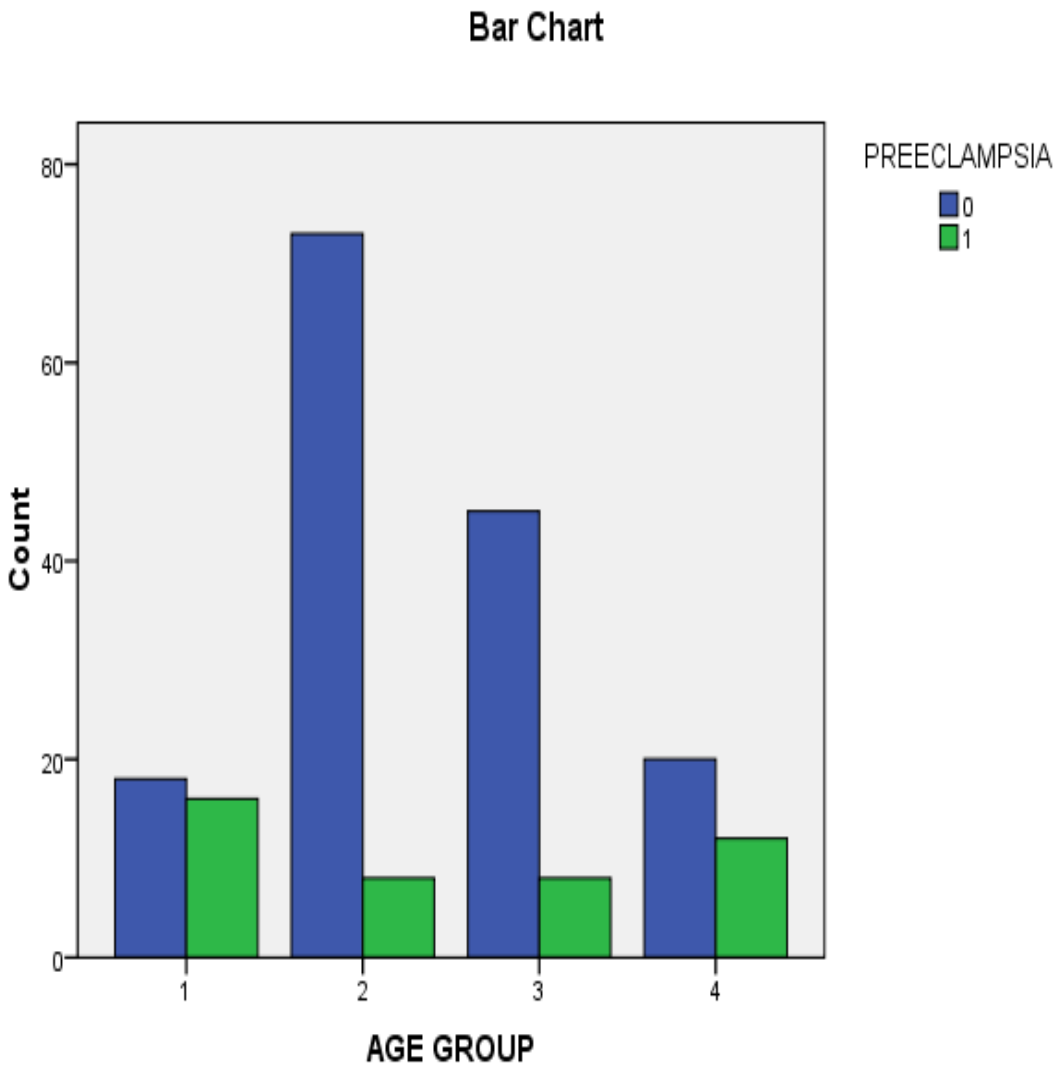
- Age group distribution shows , 36.4 % of pre-eclampsia cohort and 11.5 % of normal cohort belongs to age group

  < 20 .

- 27.3 % of pre-eclampsia cohort and 12.8 % of normal cohort belongs to age group > 30 .

- It showed that pre - eclampsia is more common in teenage and in elderly gravid.

AGE GROUP – DISTRIBUTION AMONG STUDY POPULATION



0=normal cohort 1=preeclamptic cohort

1- <20yrs ; 2- 21 to 25 yrs ; 3- 26 to 30 yrs ; 4- > 30 yrs.

INFERENCE:

As ‘p’ value is 0.000,there is statistically significance between pre-eclampsia cohort and normal cohort with regard to age group.

OBSTETRIC SCORE - OCCURRENCE OF PREECLAMPSIA

Crosstab					
			PREECLAMPSIA		
			0	1	Total
PARITY	1	Count	80	32	112
		% within PREECLAMPSIA	51.3%	72.7%	56.0%
		% of Total	40.0%	16.0%	56.0%
	2	Count	70	10	80
		% within PREECLAMPSIA	44.9%	22.7%	40.0%
		% of Total	35.0%	5.0%	40.0%
	3	Count	6	2	8
		% within PREECLAMPSIA	3.8%	4.5%	4.0%
		% of Total	3.0%	1.0%	4.0%
	Total	Count	156	44	200
		% within PREECLAMPSIA	100.0%	100.0%	100.0%
		% of Total	78.0%	22.0%	100.0%

Table no 8

Chi square value - 7.068 p value - 0.029

This is statistically significant.

PERCENTAGE DISTRIBUTION OF PREECLAMPSIA AMONG PRIMI GRAVIDA AND MULTI GRAVIDA

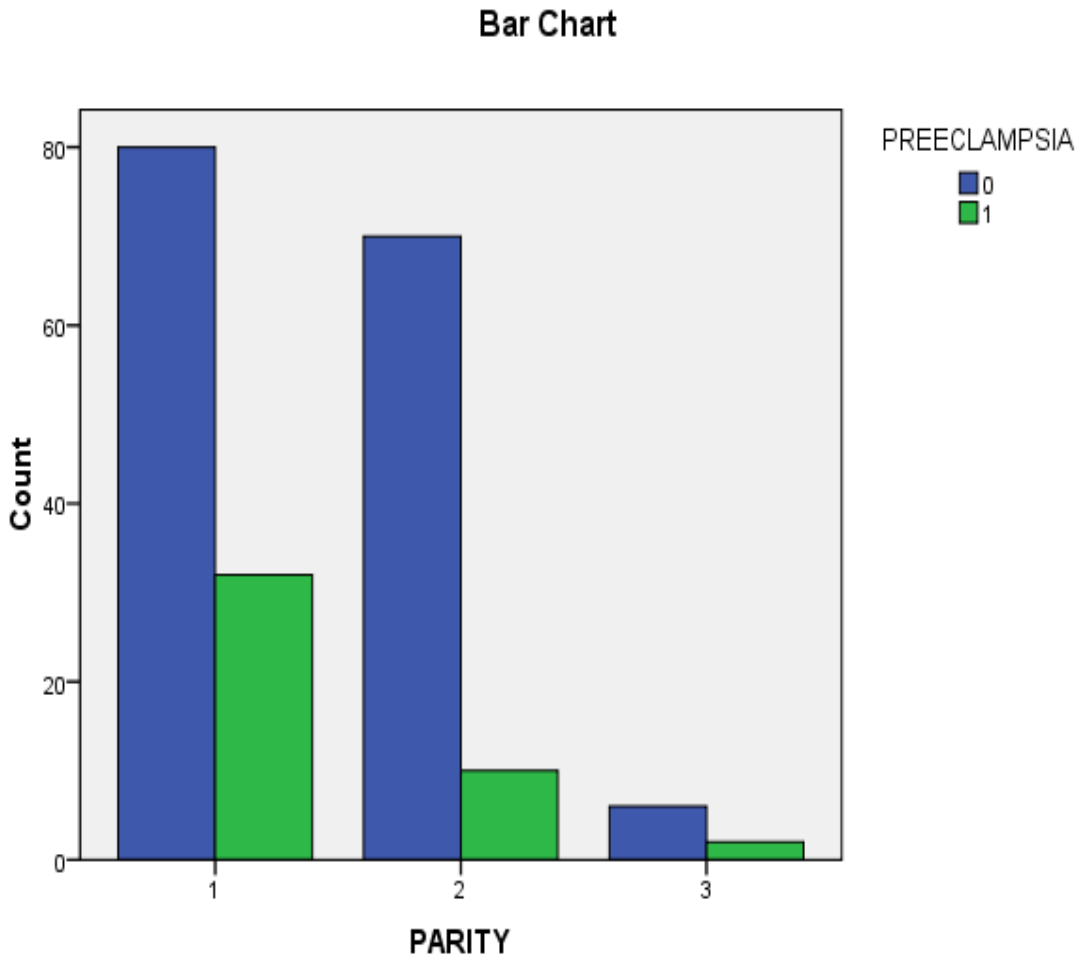
OBSTETRIC SCORE	**PRE-ECLAMPSIA COHORT**		**NORMAL COHORT**	
	NO OF CASES	**%**	**NO OF CASES**	**%**
1	32	72.7 %	80	51.3 %
2	10	22.7 %	70	44.9 %
3	2	4.5 %	6	3.8 %

Table no 9

Regarding parity

- 72.7 % of pre-eclampsia occurred in primi gravida.
- 22.7 % of pre-eclampsia occurred in second gravida
- 4.5 % of pre-eclampsia occurred in third gravida

OBSTETRIC SCORE – DISTRIBUTION OF PREECLAMPSIA AMONG STUDY GROUP



0=normal cohort 1=preeclamptic cohort

1- primi ; 2- second gravida ; 3- third gravida.

INFERENCE

- As the p value is 0.029, there is statistical significance between parity and occurrence of pre-eclampsia.

- It showed that pre-eclampsia is more common in primi gravida than in second and third gravid.

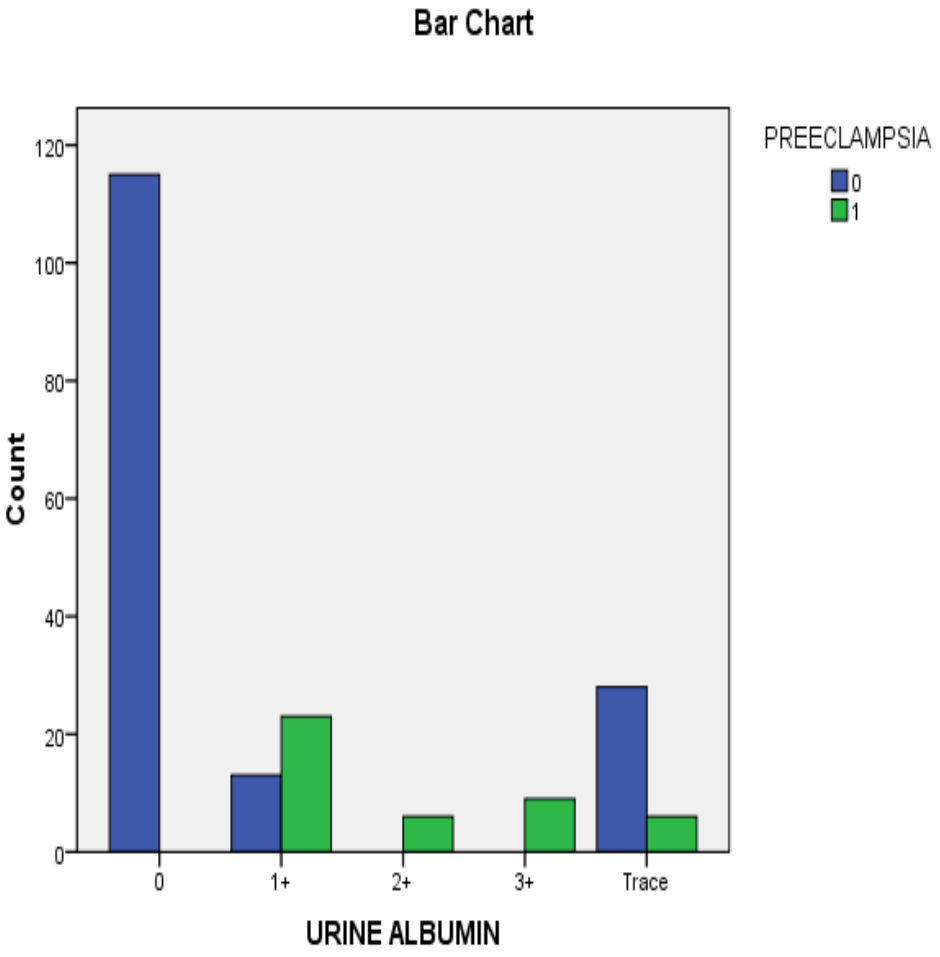
URINE ALBUMIN * PREECLAMPSIA

Crosstab					
			PREECLAMPSIA		
			0	1	Total
URINE ALBUMIN	0	Count	115	0	115
		%within PREECLAMPSIA	73.7%	.0%	57.5%
		% of Total	57.5%	.0%	57.5%
	1+	Count	13	23	36
		%within PREECLAMPSIA	8.3%	52.3%	18.0%
		% of Total	6.5%	11.5%	18.0%
	2+	Count	0	6	6
		%within PREECLAMPSIA	.0%	13.6%	3.0%
		% of Total	.0%	3.0%	3.0%
	3+	Count	0	9	9
		%within PREECLAMPSIA	.0%	20.5%	4.5%
		% of Total	.0%	4.5%	4.5%
	Trace	Count	28	6	34
		%within PREECLAMPSIA	17.9%	13.6%	17.0%
		% of Total	14.0%	3.0%	17.0%
	Total	Count	156	44	200
		%within PREECLAMPSIA	100.0%	100.0%	100.0%
		% of Total	78.0%	22.0%	100.0%

Table no 10

Chi square value - 122.805 p value - 0.000 , this is significant.

OCCURENCE OF ALBUMINURIA IN PRE - ECLAMPSIA



- Urine albuminuria of 1+ occurs in 52.3% of pre-eclampsia cases , 2+ occurs in 13.6 % and 3+ occurs in 20.5 %. of pre-eclampsia cases.

- This signifies that albuminuria is a useful index in the diagnosis of pre-eclampsia.

BMI * PRE ECLAMPSIA

BMI GROUP * PREECLAMPSIA Crosstabulation					
			PREECLAMPSIA		
			0	1	Total
BMI GROUP	1	Count	86	2	88
		% within PREECLAMPSIA	55.1%	.4.5.%	44%
		% of Total	43.0%	.1%	44%
	2	Count	51	14	65
		% within PREECLAMPSIA	32.7%	31.8%	32.5%
		% of Total	25.5%	7%	32.5%
	3	Count	12	23	35
		% within PREECLAMPSIA	7.7%	52.3%	17.5%
		% of Total	6%	11.5%	17.5%
	4	Count	7	5	12
		% within PREECLAMPSIA	4.5%	11.4%	6%
		% of Total	3.5%	2.5%	6%
	Total	Count	156	44	200
		% within PREECLAMPSIA	100.0%	100.0%	100.0%
		% of Total	78%	22%	100.0%

Table no 11

Chi square value - 65.007 p value < 0.0001

This is statistically significant correlation

BMI – DISTRIBUTION OF PREECLAMPSIA

BMI	PRE ECLAMPSIA COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
1	2	4.5 %	86	55.1 %
2	14	31.8 %	51	32.7 %
3	23	52.3 %	12	7.7 %
4	5	11.4 %	7	4.5 %

Table no 12

1- Healthy weight 2- over weight 3- Moderate obesity 4- Severe obesity.

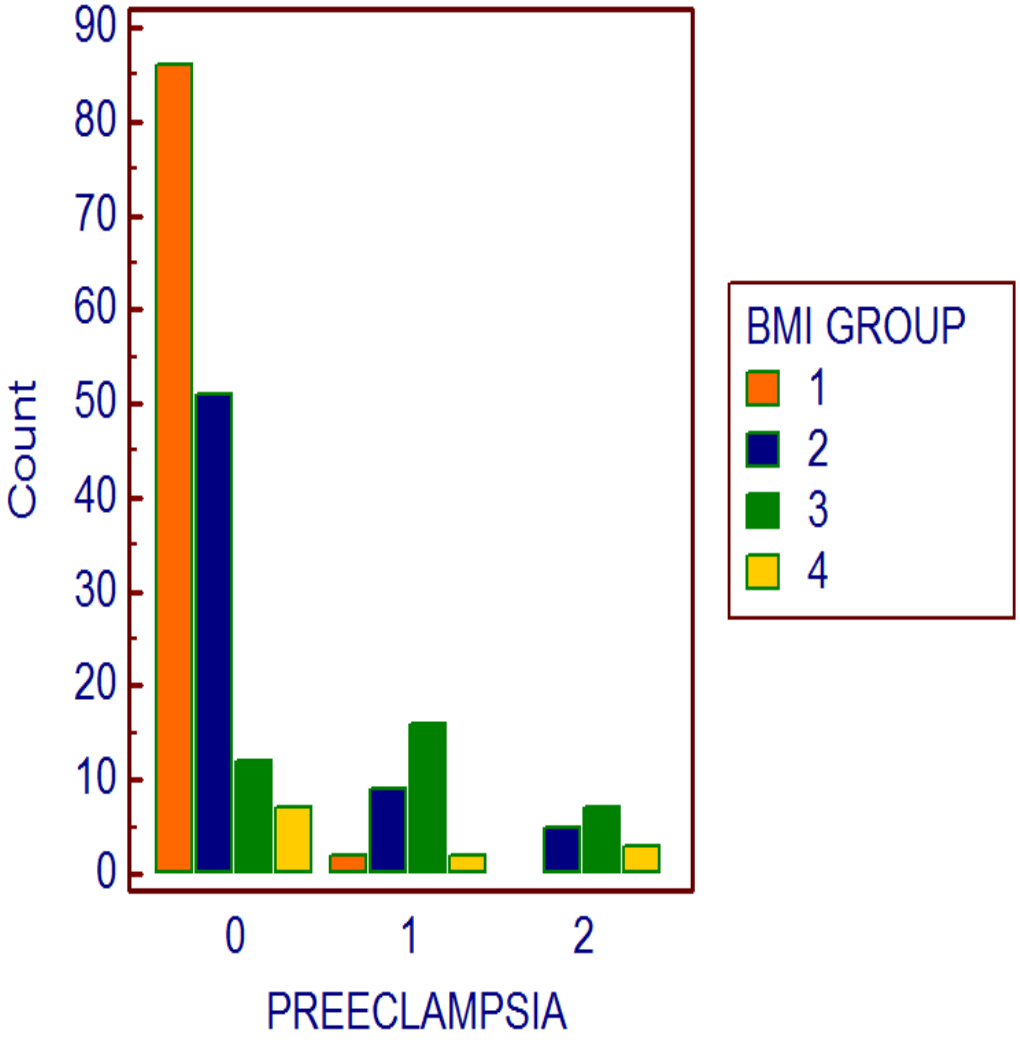
BMI of the study population was calculated according to her pre pregnant weight.

- Quetelet index was used to calculate the BMI
- From the above table it is clear that, about 52.3% of pre-eclampsia occurred in the moderately obese group
- 31.8% of pre-eclamptic cohort and 32.7% of normal cohort, were

present in overweight group.

- In women with normal BMI ,pre-eclampsia occurred in 4.5% and 55.1% comes under normal cohort

BMI - DISTRIBUTION OF PREECLAMPSIA AMONG STUDY GROUP



0- no pre eclampsia ; 1- mild pre eclampsia ; 2- severe pre eclampsia.

INFERENCE:

As p< 0.0001,there is statistical significance between, pre-eclampsia cohort and normal cohort, with regard to BMI.

SOCIOECONOMIC CLASS * PREECLAMPSIA

Crosstab

			PREECLAMPSIA		
			0	**1**	**Total**
SOCIOECONOMIC CLASS	2	Count	2	2	4
		%within PREECLAMPSIA	1.3%	4.5%	2.0%
		% of Total	1.0%	1.0%	2.0%
	4	Count	50	10	60
		%within PREECLAMPSIA	32.1%	22.7%	30.0%
		% of Total	25.0%	5.0%	30.0%
	5	Count	104	32	136
		%within PREECLAMPSIA	66.7%	72.7%	68.0%
		% of Total	52.0%	16.0%	68.0%
	Total	Count	156	44	200
		%within PREECLAMPSIA	100.0%	100.0%	100.0%

Crosstab					
			PREECLAMPSIA		
			0	**1**	**Total**
SOCIOECONOMIC CLASS	2	Count	2	2	4
		%within PREECLAMPSIA	1.3%	4.5%	2.0%
		% of Total	1.0%	1.0%	2.0%
	4	Count	50	10	60
		%within PREECLAMPSIA	32.1%	22.7%	30.0%
		% of Total	25.0%	5.0%	30.0%
	5	Count	104	32	136
		%within PREECLAMPSIA	66.7%	72.7%	68.0%
		% of Total	52.0%	16.0%	68.0%
	Total	Count	156	44	200
		%within PREECLAMPSIA	100.0%	100.0%	100.0%
		% of Total	78.0%	22.0%	100.0%

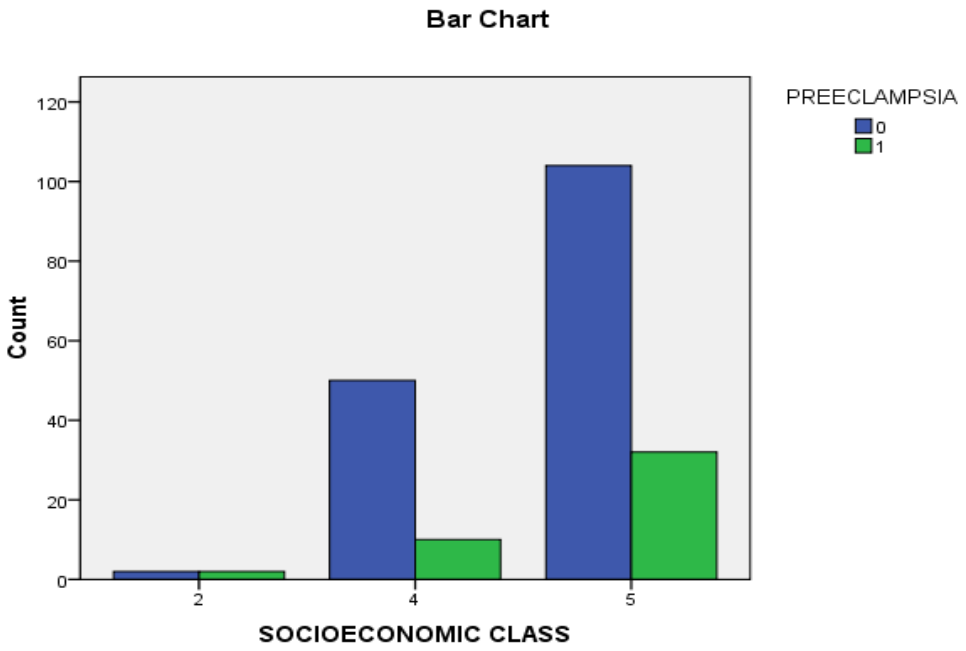
Chi square value - 3.007 : p value - 0.222.There is no statistical significance

SE CLASS - OCCURRENCE OF PREECLAMPSIA

SOCIO ECONOMIC STATUS	PRE ECLAMPSIA COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
2	2	4.5 %	2	1.3 %
4	10	22.7 %	50	32.1 %
5	32	72.7 %	104	66.7 %

About 72.7 % of the pre-eclamptic women belonged to socioeconomic class 5, 22.7 % belonged to class 4 socioeconomic status and 4.5 % belonged to class 2 socioeconomic status.

SE CLASS – DISTRIBUTION OF PREECLAMPSIA



0=normal cohort 1=preeclamptic cohort

When SE class was taken into consideration,66.7 % of normal cohort and 72.7 % of pre eclampsia cohort occurred in the class 5,whereas,32.1% of normal cohort and 22.7 % of pre eclampsia cohort belonged to class 4 SE class.

INFERENCE:

Since, the p- valve is 0.222, there is no statistical significance between pre eclampsia cohort and normal cohort with regard to socioeconomic class.

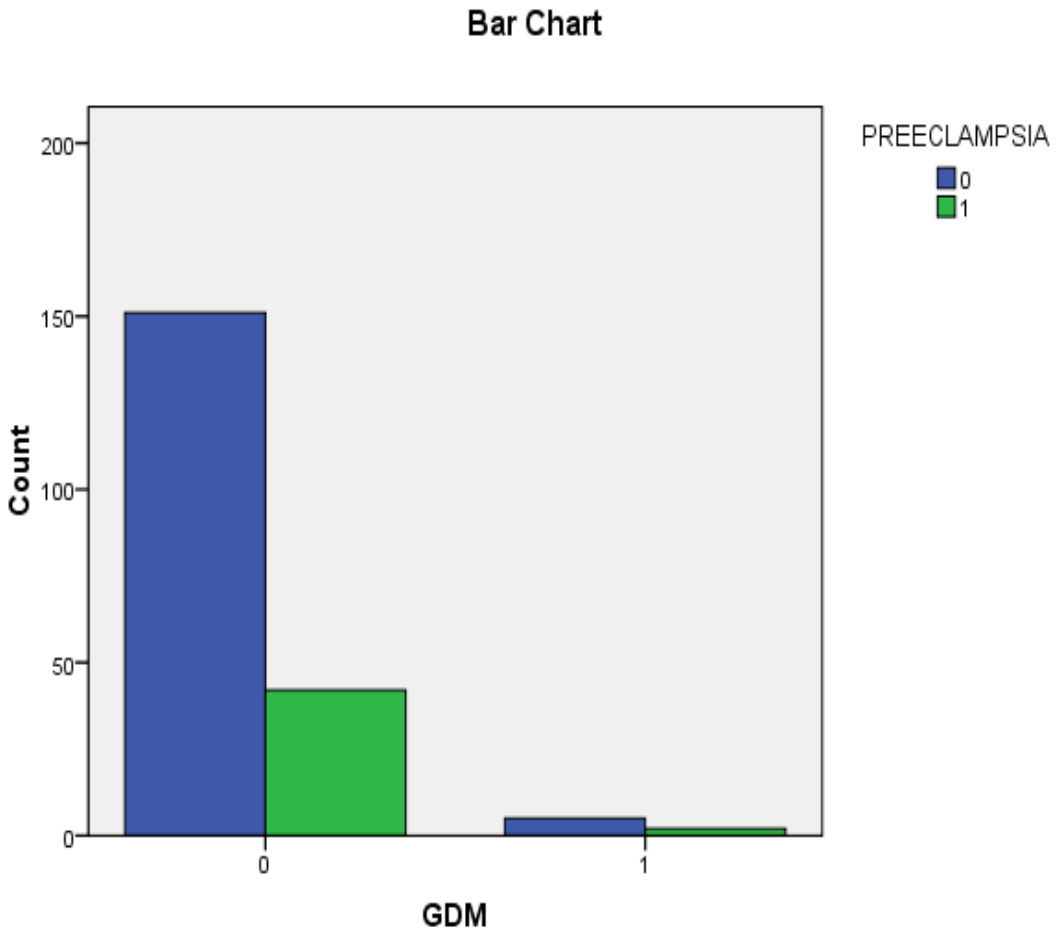
GDM * PREECLAMPSIA

Crosstab					
			PREECLAMPSIA		
			0	1	Total
GDM	0	Count	151	42	193
		% within PREECLAMPSIA	96.8%	95.5%	96.5%
		% of Total	75.5%	21.0%	96.5%
	1	Count	5	2	7
		% within PREECLAMPSIA	3.2%	4.5%	3.5%
		% of Total	2.5%	1.0%	3.5%
	Total	Count	156	44	200
		% within PREECLAMPSIA	100.0%	100.0%	100.0%
		% of Total	78.0%	22.0%	100.0%

Chi square value - 183 p value - 0.669

GDM	PRE ECLAMPSIA COHORT		NORMAL COHORT	
	No OF CASES	%	No OF CASES	%
0	42	95.5%	151	96.8%
1	2	4.5%	5	3.2%

ASSOCIATION BETWEEN PRE-ECLAMPSIA AND GDM

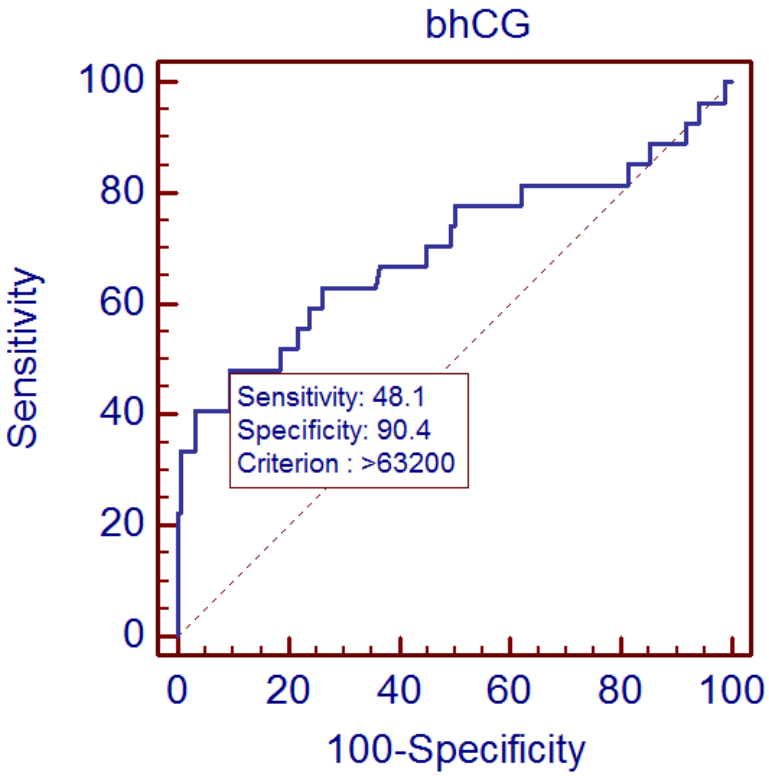


- GDM occurs in 4.5 % of pre eclampsia cohort and 3.2 % of normal cohort.

- since p value is 0.669 there is no significant association between GDM and pre eclampsia.

ROC CURVE - b hCG

Normal vs mild pre eclampsia



ROC curve for b hCG as a predictor in cases of mild pre eclampsia

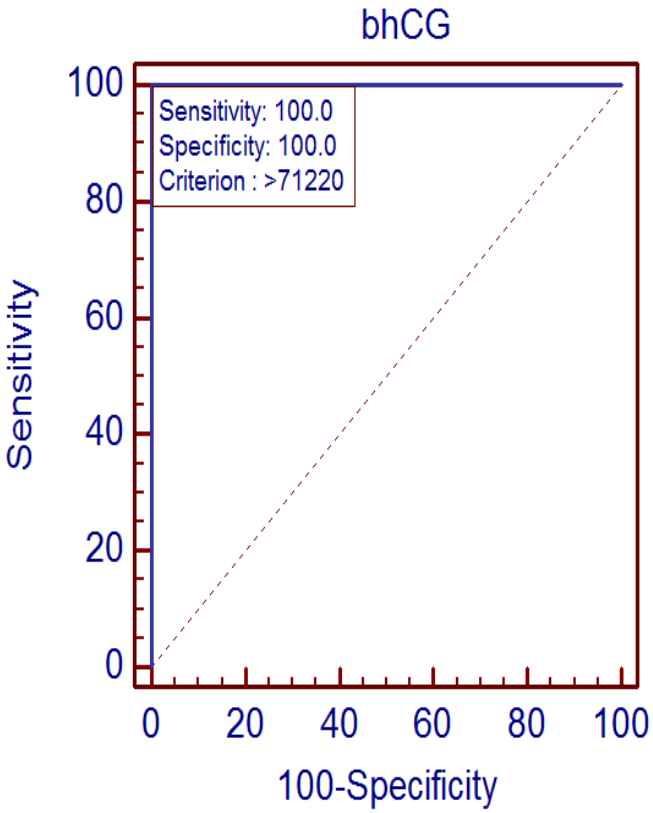
- Area under the ROC curve (AUC) 0.6993
- Standard Error 0.0678
- 95% confidence interval 0.627284 to 0.764752
- z statistic 2.941

- Significance level P (Area = 0.5) <0.0033

- The above table & ROC, infer that in the prediction of mild pre eclampsia for the cut off value >63200 ,the Area Under the ROC curve(AUC) is 0.6993. Sensitivity is 48.1 and specificity is 90.4.

ROC CURVE - b hCG

Normal vs. Severe pre eclampsia



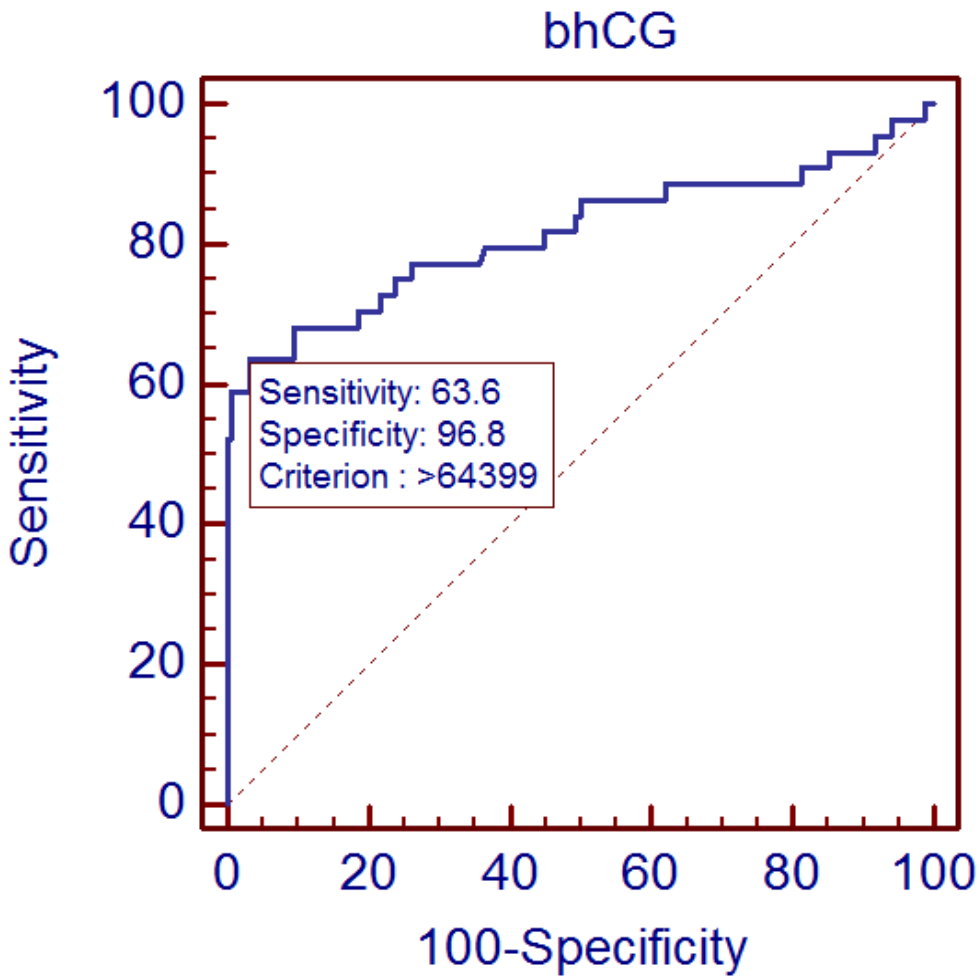
ROC curve for b hCG as a predictor in cases of severe pre eclampsia

ROC curve for b hCG as a predictor in cases of severe pre eclampsia

- Area under the ROC curve (AUC) is 1
- Standard Error 0.0000
- 95% confidence interval 0.978534 to 1.000000
- Significance level P (Area = 0.5) <0.0001
- The above table & ROC, infer that in the prediction of severe pre eclampsia for the cut off value > 71220 ,the Area Under the ROC curve(AUC) is 1. Sensitivity is 100 and specificity is 100.It indicates that b hCG is the good indicator for prediction of severe pre eclampsia.

ROC - b hCG

NORMAL VS PRE ECLAMPSIA



ROC curve for b hCG as a predictor of pre eclampsia

- Area under the ROC curve (AUC) is 0.815487
- Standard Error 0.0000
- 95% confidence interval 0.978534 to 1.000000

- Significance level P (Area = 0.5) <0.0001

- The above table & ROC, infer that in the prediction of pre eclampsia for the cut off value > 64399 ,the Area Under the ROC curve(AUC) is 0.815487. Sensitivity is 63.6 % and specificity is 96.8 % .

- It indicates that b hCG is good in predicting severe pre eclampsia than mild pre eclampsia.

Area Under a Receiver Operating Characteristic Curve (ROC):

Total area under ROC curve is used as a single index for measuring the performance a test. When the AUC is larger, the better is overall performance of the medical test to correctly identify diseased and nondiseased subjects.

When the AUCs of two tests are equal, it represents similar overall performance of tests but this does not necessarily mean that both the curves are identical. It indicates that they may cross each other.

- Regarding b hCG values, in predicting mild pre eclampsia with the cut off value > 63200 the Sensitivity is 48.1% and specificity is 90.4%.

- In predicting severe pre eclampsia with the cut off value > 71220 , the sensitivity is 100 % and specificity is 100%.

- In predicting pre eclampsia with the cut off value > 64399 ,Sensitivity is 63.6 % and specificity is 96.8 % .

- It indicates that b hCG is a good predictor of pre eclampsia, but it is a better predictor of severe pre eclampsia than mild pre eclampsia.

Group Statistics					
PREECLAMPSIA		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
AGE	1	44	24.73	4.990	.752
	0	156	24.68	3.551	.284

t test - 0.072 p - 0.943

Since p value is > 0.05 age has no significance in pre eclampsia

MULTIVARIATE ANALYSIS

Group Statistics					
PREECLAMPSIA		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
HEIGHT	1	44	152.95	4.720	.712
	0	156	156.35	5.589	.447
WEIGHT	1	44	72.23	7.924	1.195
	0	156	62.95	6.839	.548
BMI	1	44	30.897	3.3999	.5126
	0	156	25.828	3.2547	.2606

HEIGHT

t test - 3.671 p value - 0.000

Since the p value is < 0.05 height has statistical significance in pre eclampsia.

WEIGHT

t test - 7.668 p value - 0.000

since the p value is < 0.05 weight has statistical significance in pre eclampsia.

BMI

t test - 9.086 p value - 0.000

since the p value is < 0.05 BMI has statistical significance in pre eclampsia.

Group Statistics					
PREECLAMPSIA		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
STRESS SCORE	1	44	12.25	17.241	2.599
	0	153	4.42	5.728	.463

t test - 4.792 p value - 0.000

since p value < 0.05 stress has statistically significant correlation with pre eclampsia

Group Statistics					
PREECLAMPSIA		**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
bhCG	1	44	87104.09	34810.743	5247.917
	0	156	54401.45	7129.722	570.835

t test - 11.007 p value - 0.000

since p value < 0.05 b hCG has statistical significance with pre eclampsia

From this study, it was found that the following variables are statistically significant.

- Age of the patient
- Obstetric score
- Socioeconomic class
- Pre pregnancy weight of the patient and BMI

- Stress score

- Serum b hCG

OUTCOME OF THE STUDY

VARIABLE	CHI SQUARE VALUE	P VALUE
AGE	25.333	0.000
PARITY	7.068	0.029
SE CLASS	3.007	0.222
BMI	32.341	0.000

Serum b hCG has significant p value 0.000

RESULTS OF THE STUDY

Our study population included 200 antenatal women who attended antenatal out- patient department in kilpauk medical college and were completely followed till term. Among them ,serum b hCG predicted pre-eclampsia in 44 patients.

From this study it was found that, there is a statistical significance between pre-eclampsia cohort and normal cohort with regard to the following variables :

- Age
- Obstetric score
- Socioeconomic class
- BMI
- Serum beta HCG

- When age group was taken into consideration, about 36.4% developed Pre-eclampsia and 11. 5% did not develop pre-eclampsia in the age group <20 years.

- In the age group >30 years,27.3% developed pre-eclampsia and 12.8% did not develop pre-eclampsia.

- There was statistical significance (p 0.000) between normal cohort and pre-eclampsia cohort with respect to age

- The occurrence of pre eclampsia is common in teenage and elderly

- 72.7 % of pre-eclampsia occurred in primigravida , 22.7 % of pre-eclampsia occurred in second gravida and4.5 % of pre-eclampsia occurred in third gravida

- There is statistical significance (p- 0.029) between pre eclampsia and obstetric score. Pre eclampsia is more common among primigravida than in second and third gravida.

- When Socioeconomic class was taken into consideration, 72.7 % of pre-eclampsia cohort occurred in the class 5 and 22.7 % of pre-eclamptic cohort belonged to class 4 socioeconomic class. There is no statistical significance with regard to SE class.

- When BMI is taken about 52.3% of pre-eclampsia occurred in the moderately obese group 31.8% of pre-eclamptic cohort were in overweight group and 4.5 % in normal BMI group.

- The variable BMI is also statistically significant.

- With the cut off value of b hCG value > 63200 for predicting mild pre eclampsia ,the Sensitivity is 48.1% and specificity is 90.4%. It has low sensitivity and high specificity in predicting mild pre eclampsia.

- With the cut off value of b hCG > 71220 for predicting severe pre eclampsia , the sensitivity is 100 % and specificity is 100%. It has good sensitivity and specificity in predicting severe pre eclampsia.

DISCUSSION

- In this study we found that serum b hcg were elevated in pre eclampsia, more significantly elevated in severe pre eclampsia when compared with controls. This indicates that there exists an abnormal secretory functions of the placenta in cases of pre eclampsia.

- In our study 44 develop pre eclampsia among 200 subjects who were enrolled and followed.With the cut off value of b hCG value > 63200 the Sensitivity is 48.1% and specificity is 90.4% for predicting pre eclampsia .

- With the cut off value of b hCG > 71220 the sensitivity is 100 % and specificity is 100% for predicting pre eclampsia . It has good sensitivity and specificity in predicting severe pre eclampsia.

- Our study was supported by desai and rao[47,39] , 62 cases out of 90 (68.9%) with value > 2 mom developed pre eclampsia against 21 cases out of 130 (16.5%) who had beta hcg < 2mom. The difference wa statistically significant.

- Study conducted by Roiz Hernandez et al[48,49] showed that with the cut off value of 2 mom for serum beta hcg in multigravida and primigravida during second trimester , the area below roc curve was 0.96 and 0.95, respectively , its sensitivity was 88.5% and 100% respectively . The positive predictive value was 0.45 and 0.25 repectivelyand the negative predictive value was 0.99 and 1.0.

- In the present study , the elevated b hcg levels (miu/ml) showed direct association with pre eclampsia.

CONCLUSION

This study showed that measuring serum beta hcg in early second trimester at (13-20weeks) is a useful indicator to identify women who are likely to develop pre eclampsia in the same pregnancy. Also higher levels are associated with increased severity of pre eclampsia.

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APPENDIX-1

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு : **"A STUDY ON PREDICTION OF PREECLAMPSIA BY MATERNAL SERUM BETA HCG LEVELS IN EARLY SECOND TRIMESTER (13 TO 20 WEEKS) OF PREGNANCY - A COHORT STUDY "**Department of Obstetrics and Gynaecology, KMCH

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் வயது : **பங்கு பெறுபவரின் எண் :**

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. நான் இவ்வாய்வில் தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளல்லாம் என்றும் அறிந்து கொண்டேன்.இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்கமாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.பங்கேற்பவரின் கையொப்பம்

இடம் :

தேதி :

பங்கேற்பவரி ஆய்வாளரின் கையொப்பம்

ஆய்வாளரின் கையொப்பம்

PROFORMA

- NAME: HEIGHT -
- AGE: WEIGHT -
- DATE OF VISIT BMI -
- IP NO:
- SOCIO ECONOMIC STATUS
- EDUCATION
- ADDRESS
- OBSTETRIC SCORE
- LMP
- EDD
- EARLY USG EDD
- GESTATIONAL AGE
- LINICAL EXAMINATION- General examination ,Vitals (Pedal edema, Blood pressure)

- Systemic examination

Cardiovascular system

Respiratory system

Abdominal examination

- LAB INVESTIGATION

BASIC INVESTIGATIONS - (COMPLETE BLOOD COUNT,RENAL FUNCTION TESTS,URINE ROUTINE)

SERUM BETA HCG

URINE ALBUMIN

ORAL GLUCOSE CHALLENGE TEST

- STRESS SCORE

MASTER CHART

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Revathy	22	160	62	24.21	2	1	14	55,332	0	110	70	nil	0	5
kamala	20	156	58	23.8	2	1	15	64,399	0	110	70	NIL	0	5
Usha	26	154	76	31.2	4	2	14	63,550	0	120	80	NIL	0	4
Hemalatha	25	145	54	25.68	0	2	16	56,721	0	110	70	nil	0	5
Maheswari	24	152	56	24.2	10	1	14	54,280	0	120	80	Trace	0	4
seetha	23	146	70	32.8	0	1	16	61,428	0	130	70	nil	0	5
Gomathi	27	158	58	23.23	1	2	18	54,900	0	120	80	nil	0	4
Sumathi	24	146	55	25.8	1	1	16	63,410	0	110	70	nil	0	5
Mohana	26	150	80	35.55	2	2	17	43,633	0	120	80	nil	0	5
Vasanthi	22	155	78	32.5	0	1	14	50,944	0	110	70	nil	0	4
Subre nisha	22	156	58	23.8	0	1	14	41,566	0	120	80	nil	0	5
Rajalakshmi	26	145	70	33.3	1	2	16	62,554	0	110	70	1+	0	5
Mangalam	24	160	61	23.8	1	1	18	38,310	0	110	80	nil	0	4
Muthuselvi	26	144	68	32.8	1	2	17	48,966	0	120	80	Trace	0	5
Mohanapriya	21	154	63	26.56	0	1	16	61,320	0	120	80	nil	0	5
Saraswathi	25	160	58	22.6	0	1	15	52,110	0	110	80	nil	0	4
Bavani	23	162	57	21.7	2	1	15	48,300	0	120	70	nil	0	4
Tamilarasi	26	150	60	26.66	2	2	16	46,822	0	110	70	Trace	0	5
Jothi	19	152	56	24.2	0	1	14	53,440	0	120	70	1+	0	5
Eswari	20	150	52	23.1	0	1	15	40,358	0	130	80	Trace	0	4
Dhanam	28	146	76	35.6	2	2	14	50,869	0	120	70	nil	0	4
Fathima	26	156	78	32.05	2	2	16	48,994	0	120	70	nil	0	5
Yogalakshmi	26	145	67	31.86	14	1	16	47,844	0	110	70	nil	0	4
Rajeswari	26	146	56	26.2	0	2	18	56,134	0	110	80	Trace	0	5

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Abirami	27	152	72	31.6	2	2	16	58,622	0	120	70	1+	0	4
Lalitha	20	148	68	31.04	0	1	17	45,822	0	120	70	nil	0	5
Kanimozhi	26	150	69	30.7	4	2	14	46,330	0	120	80	nil	0	4
Chithra	28	152	82	35.5	16	2	15	56,440	0	110	80	nil	0	5
Bairavi	22	148	66	30.13	4	1	14	53,958	0	110	70	nil	0	5
Selvi	27	160	60	23.4	0	2	15	52,330	0	120	80	nil	0	4
Shanthi	28	150	70	31.1	2	2	16	60,498	0	110	70	nil	0	4
Ambika	26	165	62	22.7	1	1	17	54,678	0	110	70	Trace	0	4
Devika	31	162	68	25.91	15	2	16	38,890	0	120	80	Trace	0	5
Alamelu	29	164	62	23.05	0	2	14	45,678	0	120	80	1+	0	4
Ellammal	25	166	64	23.2	2	1	16	63,200	1	120	70	nil	0	4
Vaishnavi	31	150	80	35.55	16	2	16	44,580	0	110	80	nil	0	5
Vinitha	20	155	65	27.05	1	1	14	60,550	0	120	70	nil	0	5
Divya	20	162	62	23.6	0	1	16	58,940	0	110	70	nil	0	5
Buvana	29	164	67	24.91	0	2	16	45,660	0	120	80	nil	0	4
Sudha	32	155	64	26.6		2	17	52,450	0	120	80	nil	0	5
Priya	26	162	62	23.6	2	2	16	51,422	0	120	70	nil	0	4
Kavitha	31	158	60	24.03	18	2	14	50,896	0	110	80	nil	0	5
Malarvizhi	22	160	70	27.34	1	1	16	55,966	0	120	70	Trace	0	5
Punitha	26	158	60	24.03	1	2	18	64,334	1	120	70	nil	0	5
Rekha	21	160	58	22.65	3	1	15	61,613	0	110	80	nil	0	5
Narmada	22	155	64	26.63	4	1	16	56,980	0	110	70	nil	0	4
Thenmozhi	23	152	54	23.37	1	1	17	54,455	0	120	70	Trace	0	5
Nirmala	32	155	59	24.6	0	2	16	52,887	0	120	80	nil	0	5
Sasikala	26	147	56	25.91	14	2	15	45,943	0	110	80	nil	0	2
Janani	19	150	52	23.11		1	14	71,220	0	120	70	nil	0	5

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Raga priya	24	162	62	23.6	2	1	14	56,544	0	120	70	1+	0	4
Ganga lakshmi	27	158	65	26.03	0	2	15	43,548	0	110	80	Trace	0	5
Sathya	20	160	60	23.43	1	1	16	52,540	0	110	70	NIL	0	5
Gowri	25	157	56	22.71	16	1	16	46,432	0	120	80	nil	0	5
Kanniammal	22	162	70	26.7	2	1	17	51,320	0	130	70	nil	0	4
Savithri	21	155	54	22.5	3	1	16	57,310	0	130	80	nil	0	5
Sankari	20	153	55	23.4	0	1	16	61,203	0	120	70	1+	0	4
Indumathi	31	145	60	28.5	4	2	14	56,328	0	120	80	Trace	0	5
Madhavi	21	160	56	21.8	18	1	18	53,485	0	110	80	nil	0	4
Vanaja	21	165	62	22.7	4	1	14	48,446	0	120	70	nil	0	5
Banupriya	27	155	64	26.6	0	2	14	51,438	0	120	80	nil	0	4
Anitha	31	156	60	24.6	0	2	16	58,955	0	110	70	nil	0	5
Sangeetha	20	156	60	24.6	2	1	17	56,458	0	116	70	nil	0	5
Kasthina	26	150	60	26.7	14	2	16	54,883	0	116	70	Trace	0	5
Prema	24	164	58	21.6	1	1	17	55,384	0	120	80	nil	0	4
Kalai selvi	26	162	58	22.1	2	2	14	52,982	0	118	70	nil	0	5
Devikala	21	152	64	27.7		1	16	48,450	0	120	70	nil	0	5
Durga devi	28	160	62	24.2	0	2	16	51,883	0	116	80	nil	0	5
Jaya priya	20	162	62	23.6	1	1	15	49,366	0	110	70	nil	0	5
Suryakala	21	160	70	27.3	15	1	14	54,892	0	120	70	nil	0	4
Priyadarshini	23	156	86	35.33	4	1	16	48,455	0	110	80	1+	0	5
Bebi john	27	160	62	24.2	1	2	16	52,590	0	120	80	1+	0	5
Indumaheswari	21	155	65	27.05	0	1	17	56,322	0	110	80	Trace	0	5
Rajeswari	30	161	62	23.9	16	2	15	46,852	0	114	80	nil	0	5
Parimala	22	160	60	23.4	2	1	16	53,948	0	116	80	nil	0	4
Mahalakshmi	26	162	70	26.7	2	2	18	61,455	0	120	70	nil	0	5

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Jamuna rani	21	158	60	24.03	1	1	15	49,189	0	118	80	nil	0	5
Vidhya	26	160	60	23.4	1	2	16	48,966	0	110	80	nil	0	5
Kokila	31	155	66	27.5	18	2	15	52,402	0	116	70	nil	0	5
Kala rani	21	158	61	24.4	0	1	15	53,824	0	120	80	nil	0	4
Geetha	26	156	60	24.6	6	2	14	52,400	0	120	80	nil	0	5
Swarnalatha	21	156	67	27.5	6	1	16	56,344	0	116	80	Trace	0	5
Krishnaveni	28	155	58	24.14	4	2	18	63,955	0	120	70	nil	0	4
Logeswari	21	165	72	26.4	16	1	16	54,390	0	120	70	nil	0	5
Krithika	27	158	58	23.2	0	1	14	56,330	0	110	60	nil	0	5
Devi	26	160	65	25.3	4	2	16	51,342	0	120	70	Trace	0	5
Ragavi	21	156	65	26.7	6	1	16	52,834	0	110	70	nil	0	4
Manimegala	21	165	65	23.8	18	1	17	63,733	1	120	60	nil	0	5
Amudha	31	156	60	24.6	1	2	15	58,344	0	120	70	nil	0	5
Buela	32	153	64	27.3	2	2	16	61,244	0	120	70	1+	0	5
Ilavarasi	21	160	69	26.9	0	1	17	51,204	0	110	80	nil	0	5
Nadhiya	20	155	58	24.1	1	1	17	56,233	0	110	80	nil	0	5
Sundari	24	156	86	35.33	2	2	16	55,350	0	120	70	nil	0	4
Pavithra	26	169	78	27.3	14	2	15	51,266	0	116	70	nil	0	5
Thilagam	20	156	70	28.8	2	1	16	54,721	0	116	80	Trace	0	5
Aruna	21	148	53	24.9	6	1	18	48,211	0	120	80	nil	0	5
Deepa	24	153	58	24.8	0	1	16	54,204	0	120	70	nil	0	5
Kalaivani	24	158	66	26.4	2	2	16	50,266	0	110	70	Trace	0	5
Renuka	26	160	72	28.1	18	2	17	52,198	0	120	70	nil	0	4
Parvathy	23	164	74	27.5	1	1	14	49,355	0	116	70	nil	0	5
Venipriya	24	156	59	24.2	0	2	16	46,490	0	116	80	NIL	0	5
Shobana	21	150	53	23.55	5	1	18	56,344	0	118	80	NIL	0	5

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Suganthi	24	156	63	25.8	18	2	14	51,344	0	120	70	NIL	0	5
Deivanai	23	160	63	24.6	7	2	16	46,780	0	110	60	nil	0	5
Akila	31	168	58	20.5	2	2	14	56,210	0	120	70	nil	0	4
Bindhu	24	160	68	26.5	0	1	16	53,466	0	110	60	nil	0	5
Barathi	22	158	58	23.2	2	1	15	49,566	0	116	60	nil	0	4
Rani	31	160	62	24.2	18	2	16	51,255	0	120	70	Trace	0	4
Farhana	25	152	65	28.1	2	1	16	56,456	0	110	80	Trace	0	5
Padma	27	156	60	24.65	4	2	18	65,485	0	120	70	Trace	0	5
Meenakshi	27	160	62	24.2	1	2	16	63,451	0	120	70	nil	0	4
Loganayaki	26	156	64	26.29	14	2	14	63,433	0	110	60	nil	0	5
Devika	31	148	54	24.7	0	2	14	58,433	0	120	70	nil	0	5
Saranya	24	154	56	23.6	2	2	16	57,460	0	116	70	nil	0	4
Deivambiga	23	160	68	26.6	0	1	16	60,341	0	110	70	Trace	0	5
Ponmalar	20	158	60	24	6	2	15	61,355	0	120	80	Trace	0	2
Tamilselvi	27	160	63	24.6	15	2	17	63,599	0	118	70	1+	0	5
Gowthami	23	160	72	28.1	10	1	15	58,466	0	118	80	nil	0	4
Vetriselvi	32	160	60	23.4	8	3	16	49,599	0	120	80	nil	0	5
Hemavathi	20	164	66	24.5	2	1	15	54,386	0	110	80	nil	0	5
Parimala devi	26	154	70	29.5	0	2	14	52,482	0	120	70	nil	0	5
Srilatha	24	164	65	24.1	16	2	18	51,688	0	110	70	nil	0	4
Anbuselvi	19	158	61	24.4	2	1	16	54,755	0	120	70	nil	0	5
Mohana	28	152	61	26.4	0	2	16	57,522	0	116	80	nil	0	5
Karthiga	22	148	54	24.7	1	1	15	63,562	0	114	70	Trace	0	4
Nandhini	23	158	58	23.2	0	1	14	54,429	0	116	70	Trace	0	5
Sivasankari	21	162	68	25.9	4	1	14	55,411	0	114	70	nil	0	5
Venkateswari	20	164	62	23.05	17	1	16	57,406	0	120	70	nil	0	5

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Mahadevi	22	165	61	22.4	2	1	16	56,908	0	118	80	nil	0	5
Latha	31	156	65	26.7	4	2	17	58,458	0	120	70	nil	0	4
Samandhi	24	166	63	22.8	0	3	17	56,431	0	116	80	1+	0	4
Kanaga	25	164	64	23.8	6	2	16	58,312	0	118	70	nil	0	5
Senthamarai	21	154	64	26.9	16	1	14	51,388	0	116	80	nil	0	5
Geethanjali	28	160	61	23.8	1	2	14	60,210	0	120	70	nil	0	4
Logambal	32	148	54	24.7	0	3	16	61,344	0	110	60	nil	0	5
Pushpa	22	150	58	25.7	1	1	16	54,344	0	120	70	1+	0	5
Thangam	23	148	47	23.97	0	1	16	62,366	0	110	60	Trace	0	5
Aruneswari	32	154	54	22.8	2	3	16	45,298	0	110	70	nil	0	4
Prathiba	26	154	65	27.4	18	2	14	56,720	0	120	80	nil	0	5
Pon Kamalam	24	150	79	35.11	6	2	14	65,436	0	110	70	nil	0	5
Sridevi	24	155	56	23.3	4	1	18	66,425	1	110	80	Trace	0	5
Lakshmi	23	156	64	26.2	2	1	16	56,721	0	110	70	nil	0	5
Janaki	21	158	58	23.2	16	1	17	59,923	0	120	70	nil	0	4
Jayalakshmi	26	148	54	24.7	1	2	16	56,720	0	120	70	nil	0	5
Manjula	25	156	65	26.7	0	2	14	61,284	0	110	70	nil	0	5
Gayathri	24	162	61	23.2	1	1	15	54,848	0	120	80	nil	0	5
Dilliammal	31	158	59	23.6	4	3	16	57,488	0	110	80	nil	0	5
Sandhiya	22	148	58	26.5	3	1	16	61,334	0	120	80	nil	0	4
Savitha rani	31	158	56	22.4	2	2	14	51,440	0	110	70	Trace	0	5
Ranjani	24	158	60	24.03	15	1	15	48,344	0	120	80	nil	0	5
Nithya veni	23	148	58	26.4	4	1	15	61,229	1	110	80	nil	0	5
Manonmani	31	162	62	23.62	4	3	14	57,282	0	120	70	1+	0	4
Shanthi devi	20	158	62	24.8	0	2	17	56,621	0	110	70	nil	0	5
Akilandeswari	25	162	70	26.7	2	1	16	56,672	0	120	80	nil	0	5

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Helen	25	164	60	22.3	12	1	17	5,674	0	120	70	nil	0	4
Radhika	24	148	58	26.4	2	1	17	65,932	0	120	70	Trace	0	4
Ramyadeepa	26	156	56	23.01	14	1	15	38,550	0	140	90	1+	1	5
Vimalochini	22	148	72	32.9	0	1	16	45,620	0	140	90	Trace	1	5
Arpudha mary	20	155	62	25.8	18	1	18	46,220	0	140	90	1+	1	5
Amsavalli	20	150	64	28.4	4	1	17	48,400	0	140	92	Trace	1	4
Vasumathi	24	152	81	35.05	6	1	16	49,100	0	130	94	1+	1	5
Vijayalakshmi	23	156	78	32.05	4	1	16	52,800	0	140	90	1+	1	5
Prasana kumari	22	160	78	30.5	15	1	15	54,824	0	130	92	1+	1	5
Srilekha	31	160	82	32.03	17	1	16	54,880	0	130	90	Trace	1	4
Kalaiarasi	25	155	82	34.13	18	1	16	55,644	0	140	94	1+	1	5
Ezhilarasi	24	156	78	32.05	0	1	16	56,544	0	140	90	1+	1	5
Subha	19	148	72	32.9	16	1	16	58,550	0	136	92	1+	1	5
Vidya lakshmi	24	150	76	33.8	18	2	15	58,343	0	140	90	Trace	1	4
Sujatha	31	152	78	33.8	1	1	14	59,212	0	136	90	1+	1	5
Thenalli	26	148	69	31.5	8	1	16	61,192	0	140	92	1+	1	5
Mala	26	154	75	31.6	14	2	15	63,220	0	140	94	1+	1	5
Vinodhini	20	160	77	30.1	6	1	16	63,288	0	134	90	1+	1	4
Parameswari	18	155	60	25	16	1	17	64,520	0	130	90	Trace	1	5
Vanitha	32	148	68	31.04	16	2	18	64,455	0	138	92	1+	1	2
Vendamalli	25	145	70	33.3	0	2	17	66,543	0	140	92	1+	1	5
Mutharasi	32	160	68	26.6	18	1	17	67,452	0	140	90	1+	1	4
Kasthri	20	144	72	34.7	16	1	16	69,100	0	138	90	1+	1	5
Sarasu	19	155	68	28.3	6	1	15	72,220	0	136	92	Trace	1	5
Nagalakshmi	20	157	61	24.7	18	1	16	74,340	0	140	90	1+	1	5
Sarala	33	146	60	28.1	0	3	16	76,843	0	140	90	1+	1	5

NAME	AGE	Height	Weight	Bmi	Stress score	Parity	GA	BHCG	GDM	SBP	DBP	Urine Albumin	Preeclampsia	Socio Economic Class
Mumtaj	31	148	77	35.2	2	2	15	78,780	0	136	92	1+	1	4
Madhuri	19	152	62	26.8	16	1	16	84,660	0	140	90	1+	1	5
Sundaravalli	20	160	72	28.12	6	1	15	93,420	0	140	90	1+	1	5
Sowmiya	26	156	84	34.5	4	1	16	1,05,300	1	138	90	1+	1	4
Koteeswari	31	148	62	28.3	16	1	17	1,12,760	0	140	90	1+	1	5
Govindammal	32	154	85	35.8	6	2	16	98,896	0	160	100	3+	2	5
Padmavathy	20	155	62	25.8	16	1	16	1,08,654	0	150	110	2+	2	5
Rajathi	26	155	78	32.4	18	1	17	1,08,986	0	160	100	3+	2	4
Usha	19	152	66	28.5	6	1	18	1,17,553	0	150	110	2+	2	5
Jayanthi	20	154	64	26.9	8	1	16	1,22.880	0	160	100	3+	2	5
Manimegalai	26	155	85	35.4	8	2	16	1,23,556	0	160	110	2+	2	5
Nagamani	19	156	68	27.9	10	1	15	1,26,722	1	150	100	3+	2	4
Lavanya	32	158	82	32.8	0	2	16	1,28,220	0	160	110	3+	2	5
Malarvizhi	19	148	78	35.6	8	1	15	1,32,860	0	160	100	3+	2	5
Kalaiselvi	19	158	74	29.6	15	1	14	1,34,450	0	150	100	3+	2	5
Ramani	31	149	72	32.4	12	3	14	1,36,786	0	160	110	2+	2	2
Gaja lakshmi	26	150	76	33.8	1	1	16	1,39,078	0	160	110	2+	2	5
Sasikala	31	148	74	33.8	16	2	15	1,45,266	0	150	100	2+	2	5
Vetriselvi	33	160	85	33.2	6	2	16	1,54,202	0	160	100	3+	2	5
Prema	26	144	65	31.3	116	1	15	1,57,711	0	160	110	3+	2	4

Preeclampsia 0 - No preeclampsia ; 1 - mild preeclampsia; 2- severe preeclampsia